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=> d his ful

     (FILE 'STNGUIDE' ENTERED AT 15:03:19 ON 12 SEP 2005)
                DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 15:06:15 ON 12 SEP 2005
                E GLYPICAN 1 /CN
L1             1 SEA ABB=ON  PLU=ON  "GLYPICAN 1 (HUMAN)"/CN
   FILE 'CAPLUS' ENTERED AT 15:06:52 ON 12 SEP 2005
L2             4 SEA ABB=ON  PLU=ON  L1
L3           109 SEA ABB=ON  PLU=ON  (GLYPICAN (2W) 1)/BI
L4          1550 SEA ABB=ON  PLU=ON  HEPAR!N/OBI(3A) SULFATE/OBI(3A) PROTEOGLYCA
                N#/OBI
L5             8 SEA ABB=ON  PLU=ON  L4 (L) GLYCOSYLPHOSPHATIDYLINOS?/OBI
L6           118 SEA ABB=ON  PLU=ON  L5 OR L2 OR L3
L7        231881 SEA ABB=ON  PLU=ON  ANTIBOD?/OBI
L8            11 SEA ABB=ON  PLU=ON  L6 AND L7
L9        174624 SEA ABB=ON  PLU=ON  ANTITUMOR?/OBI OR ANTINEOPLAS?/OBI
L10            3 SEA ABB=ON  PLU=ON  L9 AND L6
L11            1 SEA ABB=ON  PLU=ON  L8 AND L10
L12           13 SEA ABB=ON  PLU=ON  L8 OR L10 OR L11
    FILE 'BIOSIS, MEDLINE, EMBASE' ENTERED AT 15:15:11 ON 12 SEP 2005
L13          259 SEA ABB=ON  PLU=ON  L3
L14         9855 SEA ABB=ON  PLU=ON  L4
L15          127 SEA ABB=ON  PLU=ON  L14 (L) GLYCOSYLPHOSPHATIDYLINO?
L16          354 SEA ABB=ON  PLU=ON  L13 OR L15
L17      1812760 SEA ABB=ON  PLU=ON  ANTIBOD?
L18           54 SEA ABB=ON  PLU=ON  L16 AND L17
L19       626863 SEA ABB=ON  PLU=ON  ANTINEOPLAS? OR ANTITUMOR? OR ANTICANCER?
                OR ANTICARCINO?
L20            0 SEA ABB=ON  PLU=ON  L18 AND L19
L21            0 SEA ABB=ON  PLU=ON  L19 AND L16
L22      4460830 SEA ABB=ON  PLU=ON  CANCER? OR TUMOR? OR NEOPLAS? OR CARCINOM?
                OR NEOPLAS?
L23           75 SEA ABB=ON  PLU=ON  L16 AND L22
L24           15 SEA ABB=ON  PLU=ON  L17 AND L23
L25       508627 SEA ABB=ON  PLU=ON  BINDING (2W) (MOLECULE OR PROTEIN#)
L26           34 SEA ABB=ON  PLU=ON  L25 AND L16
L27            4 SEA ABB=ON  PLU=ON  L26 AND (L19 OR L22)
L28           34 SEA ABB=ON  PLU=ON  L27 OR L26
L29           16 DUP REM L28 (18 DUPLICATES REMOVED)
                     ANSWERS '1-9' FROM FILE BIOSIS
                     ANSWER '10' FROM FILE MEDLINE
                     ANSWERS '11-16' FROM FILE EMBASE


     FILE 'CANCERLIT' ENTERED AT 15:19:25 ON 12 SEP 2005
L30           13 SEA ABB=ON  PLU=ON  GLYPICAN (2W) 1
L31           12 SEA ABB=ON  PLU=ON  L14 (L) GLYCOSYLPHOSPHATIDYLINO?
L32           18 SEA ABB=ON  PLU=ON  L31 OR L30

     FILE 'CANCERLIT, BIOSIS, MEDLINE, EMBASE' ENTERED AT 15:20:34 ON 12 SEP
     2005
L33           33 DUP REM L32 L29 (1 DUPLICATE REMOVED)
                     ANSWERS '1-18' FROM FILE CANCERLIT
                     ANSWERS '19-27' FROM FILE BIOSIS
                     ANSWER '28' FROM FILE MEDLINE
                     ANSWERS '29-33' FROM FILE EMBASE
                D TI 1-10
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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:40:47 ON 12 SEP 2005
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STRUCTURE FILE UPDATES:   11 SEP 2005  HIGHEST RN 862883-42-9
DICTIONARY FILE UPDATES:  11 SEP 2005  HIGHEST RN 862883-42-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que l1
L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "GLYPICAN 1 (HUMAN)"/CN


=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   131753-81-6  REGISTRY
ED   Entered STN:  01 Feb 1991
CN   Proteoglycan, prepro- (human clone 64K3/64K4 core protein moiety reduced)
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Glypican (human clone 64K3, 64K4 )
CN   Glypican 1 (human)
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
```

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:40:57 ON 12 SEP 2005
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FILE COVERS 1907 - 12 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 11 Sep 2005 (20050911/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> fil caplus
FILE 'CAPLUS' ENTERED AT 15:40:59 ON 12 SEP 2005
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FILE COVERS 1907 - 12 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 11 Sep 2005 (20050911/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que l12
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON "GLYPICAN 1 (HUMAN)"/CN

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L2            4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1
L3          109 SEA FILE=CAPLUS ABB=ON  PLU=ON  (GLYPICAN (2W) 1)/BI
L4         3470 SEA FILE=CAPLUS ABB=ON  PLU=ON  HEPAR!N /BI (3A) SULFATE/BI
                (3A) PROTEOGLYCAN/BI
L5           50 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 (L) GLYCOSYLPHOSPHATIDYLINOS
                ?/BI
L6          151 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 OR L3 OR L2
L7       231881 SEA FILE=CAPLUS ABB=ON  PLU=ON  ANTIBOD?/OBI
L8           11 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND L7
L9       174624 SEA FILE=CAPLUS ABB=ON  PLU=ON  ANTITUMOR?/OBI OR ANTINEOPLAS?/
                OBI
L10           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND L6
L11           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L10
L12          13 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR L10 OR L11


=> d .ca l12 1-13

L12  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:451224  CAPLUS
DOCUMENT NUMBER:          142:480177
TITLE:                    Diagnosis of hyperinsulinemia and type II diabetes and
                          protection against same based on genes differentially
                          expressed in pancreas cells
INVENTOR(S):              Kopchick, John J.; Coschigano, Karen T.; Boyce, Keith
                          S.; Kriete, Andres
PATENT ASSIGNEE(S):       Ohio University, USA
SOURCE:                   PCT Int. Appl., 395 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005046718         A1    20050526    WO 2004-US36760         20041105
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
             SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       US 2003-517376P     P  20031106
                                             US 2004-579232P     P  20040615
ED   Entered STN:  27 May 2005
AB   Mouse genes differentially expressed in comparisons of normal vs.
     hyperinsulinemic, hyperinsulinemic vs. type 2 diabetic, and normal vs.
     type 2 diabetes pancreas are provided by gene chip anal., as have
     corresponding human genes and proteins.  The human mols., or antagonists
     thereof, may be used for protection against hyperinsulinemia or type 2
     diabetes.  In order to identify pancreatic genes involved in the
     development of type 2 diabetes, microarray anal. was used to compare RNA
     expression levels of 10,000 genes in pancreas of high fat diet fed and
     control diet fed mice at various time points in the progression of type 2
```

diabetes.
IC ICM A61K038-53
ICS C12Q001-68; G01N033-50; A61P003-10
CC 14-8 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 63
IT **Antibodies** and Immunoglobulins
Antisense nucleic acids
Peptide nucleic acids
Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnosis of hyperinsulinemia and type II diabetes and protection against same based on genes differentially expressed in pancreas cells)
IT **Antibodies** and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragments; diagnosis of hyperinsulinemia and type II diabetes and protection against same based on genes differentially expressed in pancreas cells)
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glypican-1**; diagnosis of hyperinsulinemia and type II diabetes and protection against same based on genes differentially expressed in pancreas cells)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:216606 CAPLUS
DOCUMENT NUMBER: 142:292452
TITLE: Compns. and methods for treating and diagnosing chronic visceral hypersensitivity and irritable bowel syndrome, based on differential gene or protein expression
INVENTOR(S): Pasricha, Pankaj; Shenoy, Mohan; Winston, John
PATENT ASSIGNEE(S): Cytokine Pharmasciences, Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020902	A2	20050310	WO 2004-US27356	20040823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005130189	A1	20050616	US 2004-923035	20040823

PRIORITY APPLN. INFO.: US 2003-496716P P 20030821
ED Entered STN: 11 Mar 2005
AB Compns. and methods for diagnosing and treating chronic visceral

hypersensitivity (CVH) and CVH-associated disorders, such as irritable bowel syndrome, are disclosed. Genes differentially expressed in CVH tissues relative to normal tissues are identified. The genes and the gene products (i.e., the transcribed polynucleotides and polypeptides encoded by the genes) can be used as markers of CVH. The genes and the gene products can also be used to screen agents that modulate the gene expression or the activities of the gene products. The examples discuss the effects of acetic acid sensitization and CNI1493 treatment on the colon and S1 dorsal root ganglia in a rat model of visceral hypersensitivity. Gene expression profiles associated with these treatments are presented, and rat CVH-related genes and polypeptides are identified.

IC ICM A61K

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 14, 63

ST treatment diagnosis irritable bowel syndrome chronic visceral hypersensitivity; sequence protein gene expression profile chronic visceral hypersensitivity rat; chronic visceral hypersensitivity diagnosis ligand **antibody** CNI1493

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glypican-1**; compns. and methods for treating and diagnosing chronic visceral hypersensitivity and irritable bowel syndrome, based on gene or protein expression profiles)

IT **Antibodies** and Immunoglobulins
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(to CVH-related proteins; compns. and methods for treating and diagnosing chronic visceral hypersensitivity and irritable bowel syndrome, based on gene or protein expression profiles)

L12 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1081081 CAPLUS
DOCUMENT NUMBER: 142:69928
TITLE: Differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening
INVENTOR(S): Ren, Ee Chee; Neo, Soek Ying
PATENT ASSIGNEE(S): Agency for Science, Technology and Research, Singapore
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108964	A1	20041216	WO 2004-SG166	20040604

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-475508P P 20030604

ED Entered STN: 17 Dec 2004
AB The invention provides genes differentially expressed in hepatocellular carcinoma (HCC) as well as DNA and protein arrays which may be used for HCC diagnosis, to assess HCC progression or regression, or the efficacy and/or toxicity of HCC therapeutics, and/or to identify candidate compds. for HCC therapy, with high predictive accuracy.
IC ICM C12Q001-68
ICS C12N015-11; C12N015-12; G06F019-00
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 14
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(J protein; differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening)
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**glypican-1**; differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(heavy chain, γ3; differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(κ-chain; differentially regulated hepatocellular carcinoma genes and protein and DNA arrays for use in diagnosis and drug screening)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:331912 CAPLUS
DOCUMENT NUMBER: 140:337340
TITLE: Molecular sub-classification of kidney tumors and the discovery of new diagnostic markers from gene expression profiles
INVENTOR(S): Teh, Bin Tean; Takahashi, Masayuki
PATENT ASSIGNEE(S): Van Andel Institute, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032842	A2	20040422	WO 2003-US31476	20031006
WO 2004032842	A3	20040930		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2501131	AA	20040422	CA 2003-2501131	20031006
EP 1570078	A2	20050907	EP 2003-781307	20031006

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	US 2002-415775P	P	20021004
	WO 2003-US31476	W	20031006

ED Entered STN: 23 Apr 2004

AB Genes that are differentially expressed in subtypes of renal cell carcinomas are disclosed as are their polypeptide products. Using a microarray comprising 18,968 cDNA probesets, about 30 mol. markers are identified as significantly (>5-fold) more highly expressed in clear cell renal cell carcinoma (CC-RCC), about 30 such mol. markers are identified for papillary-RCC, about 30 such mol. markers are identified for chromophobe-RCC/oncocytoma-RCC, about 29 such mol. markers are identified for sarcomatoid-RCC, about 74 such mol. markers are identified for transitional cell carcinoma, and about two such mol. markers are identified for Wilms' tumor. This information is utilized to produce nucleic acid and antibody probes and sets of such probes that are specific for these genes and their products. Methods employing these probes, including hybridization and immunol. methods, are used to determine the subtype of a renal cell tumor sample from a subject based on the differential expression of such genes that is characteristic of the cancer subtype.

IC ICM A61K

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 9

IT Proteoglycans, biological studies
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**glypican-1**; mol. sub-classification of kidney tumors and the discovery of new diagnostic markers from gene expression profiles)

IT **Antibodies** and Immunoglobulins
Probes (nucleic acid)
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mol. sub-classification of kidney tumors and the discovery of new diagnostic markers from gene expression profiles)

IT **Antibodies** and Immunoglobulins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(κ-chain, C region; mol. sub-classification of kidney tumors and the discovery of new diagnostic markers from gene expression profiles)

IT **Antibodies** and Immunoglobulins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(λ-chain; mol. sub-classification of kidney tumors and the discovery of new diagnostic markers from gene expression profiles)

L12 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:211992 CAPLUS
DOCUMENT NUMBER:	140:247036
TITLE:	Use of 6-amino-quinoline-5,8-quinones and nucleic acids associated with senescence for the treatment of

tumors

INVENTOR(S): Hermeking, Heiko; Lodygin, Dimitri
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1398031	A1	20040317	EP 2002-20087	20020906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004022059	A2	20040318	WO 2003-EP9884	20030905
WO 2004022059	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2002-20087 A 20020906
ED Entered STN: 17 Mar 2004
AB The present invention relates to the use of at least one 6-amino-quinoline-5,8-quinone for preparing a pharmaceutical composition for the treatment of tumors. A further subject matter of the present invention is a nucleic acid associated with senescence and its use for the treatment of tumors. In order to detect genes and pathways repressed during replicative senescence, the gene expression pattern of senescent human fibroblasts was compared to the expression signature of confluent, early passage cells. Using microarray anal., several components of the cGMP-signaling pathway were found to be downregulated during replicative senescence of primary human diploid fibroblasts (HDF). Therefore, the effect of pharmacol. inhibition of cGMP-synthesis was analyzed in HDF. 6-Anilinoquinoline-5,8-quinone (LY83583 or LY), an inhibitor of guanylate cyclase, unexpectedly induced cellular senescence. One hundred fourteen genes differentially expressed after treatment with LY were regulated similarly in HDF undergoing replicative senescence, indicating that these genes may constitute components of a transcriptional program which mediates the senescent phenotype. Among the LY-induced genes was the cdk-inhibitor p21WAF1/SDI/CIP1. In colorectal cancer cells, transcription of p21 was induced by LY in a p-53-independent manner. Furthermore, p21 but not p53, was required for cell-cycle inhibition by LY. Inactivation of the retinoblastoma tumor suppressor protein, an effector of p21-mediated cell cycle inhibition, converted LY-induced growth arrest to apoptosis. These results suggest that LY, or derivs. thereof, may be useful tumor therapeutics.
IC ICM A61K031-47
ICS A61K031-7088; A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3, 14
ST amino quinoline quinone **antitumor** agent; nucleic acid assocd

senescence treatment tumor; LY83583 guanylate cyclase inhibitor **antitumor** agent

IT **Antitumor** agents
Drug delivery systems
Fibroblast
Gene expression profiles, animal
Gene therapy
Genetic vectors
Human
(6-amino-quinoline-5,8-quinones and nucleic acids associated with senescence for treatment of tumors)

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**glypican-1**, nucleic acid encoding;
6-amino-quinoline-5,8-quinones and nucleic acids associated with senescence for treatment of tumors)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:7699 CAPLUS
DOCUMENT NUMBER: 140:198556
TITLE: Effects of dietary folate and aging on gene expression in the colonic mucosa of rats: implications for carcinogenesis
AUTHOR(S): Crott, Jimmy W.; Choi, Sang-Woon; Ordovas, Jose M.; Ditelberg, Jeremy S.; Mason, Joel B.
CORPORATE SOURCE: Vitamins and Carcinogenesis Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA, 02111, USA
SOURCE: Carcinogenesis (2004), 25(1), 69-76
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Jan 2004
AB Folate depletion and aging are risk factors for colorectal cancer. We investigated the effects of folate nutritional status and aging on gene expression in the rat colon. Young weanling and older (12 mo) rats were fed folic acid-depleted (0 mg/kg) and supplemented (8 mg/kg) diets for 20 wk. Gene expression was measured in colonic mucosal scrapings (n = 3/group) using oligonucleotide arrays (Affymetrix U34A). Folate depletion induced up-regulation of immune-related genes, urokinase, and inducible nitric oxide synthase and down-regulation of adhesion mols. (protocadherin-4, nidogen, integrin αV) and vascular endothelial growth factor in young rats. The abbreviated response to dietary folate depletion in old rats (62 changes vs. 136 in the young) included up-regulation of caspase-2 and deletion in colon cancer. Gene expression changes due to aging were more abundant in folate-depleted vs. supplemented rats (38 vs. 119 genes, resp.). In folate-deficient rats, aging induced down-regulation of immune-related genes, urokinase, p53, insulin-like growth factor binding protein-3 (IGF-BP3), and vav-1 oncogene. In folate-supplemented rats, aging induced down-regulation of vascular endothelial growth factor and caspase-2. Lower expression of adhesion mols. and higher expression of urokinase with folate depletion in young rats may indicate that cell detachment and migration (cancer-related processes) may be modulated by folate nutritional status. Age-related declines in p53 and IGF-BP3 expression was observed only in folate-depleted animals, indicating that folate supplementation may decrease the risk for age-associated cancers by suppressing deleterious changes in the expression

of certain genes.
CC 18-2 (Animal Nutrition)
Section cross-reference(s): 14
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgM; dietary folate and aging effects on gene expression in colonic mucosa of rats and implications for carcinogenesis)
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**glypican-1**; dietary folate and aging effects on gene expression in colonic mucosa of rats and implications for carcinogenesis)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:435071 CAPLUS
DOCUMENT NUMBER: 139:3235
TITLE: **Glypican-1** determination and modulation in human breast cancer diagnosis and treatment
INVENTOR(S): Korc, Murray; Lander, Arthur D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 807,575.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003103980	A1	20030605	US 2002-210327	20020731
WO 2000023109	A1	20000427	WO 1999-US24176	19991015

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1998-104510P	P	19981016
US 1999-121624P	P	19990225
WO 1999-US24176	W	19991015
US 2001-807575	A2	20010712
US 2001-309722P	P	20010731

ED Entered STN: 06 Jun 2003
AB **Glycosylphosphatidylinositol**- (GPI-) anchored **heparan sulfate proteoglycan** (HSPG) **glypican-1** is strongly expressed in human breast and pancreatic cancer-both by the cancer cells and, in the case of pancreatic cancer, the adjacent fibroblasts-whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth

factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast cancer tissues as well as breast cancer cells by comparison with breast normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EGF. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas. By immunohistochem., strong **glypican-1** immunoreactivity was present in a heterogeneous pattern in the cancer cells forming intraductal and lobular carcinomas, and in the fibroblasts surrounding the cancer cells but not in the fibroblasts that were more distant from the tumor. A moderate to strong **glypican-1** mRNA in situ hybridization signal was also present in the cancer cells, and, to a lesser extent, in the fibroblasts immediately adjacent to the cancer cells. These observations suggest that breast cancer cells produce and release **glypican-1**, and that some of the **glypican-1** present in the fibroblasts surrounding the breast cancer cells in vivo derives from the cancer cells.

IC ICM G01N033-574
ICS A61K039-395; A61K048-00
INCL 424155100; 435007230; 514044000
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 1, 14
ST **glypican 1** breast cancer diagnosis treatment
IT Syndecans
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Diagnosis
(agents, agents binding **glypican-1**; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Animal tissue
Body fluid
(anal. of; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Diagnosis
Diagnosis
(cancer; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Mammary gland, neoplasm
(carcinoma; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(digesting extracellular portion of **glypican-1**, as therapeutic agent; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT Pancreas, neoplasm
(duct cell adenocarcinoma; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT **Antitumor** agents
Fibroblast
Human
Imaging
Immunoassay
Mammary gland, neoplasm
Northern blot hybridization
Pancreas, neoplasm
(**glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT **Antibodies** and Immunoglobulins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Antisense nucleic acids
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Proteoglycans, analysis
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glypican-1**; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Immunoassay
(immunoblotting; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Immunoassay
(immunofluorescence microscopy; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Immunoassay
(immunohistochem. staining; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Nucleic acid hybridization
(in situ; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Carcinoma
(mammary; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Transformation, genetic
(of human breast cancer cells with nucleic acid altering expression of **glypican-1**; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Carcinoma
(pancreatic ductal adenocarcinoma; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT Nucleic acids
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppressing expression of extracellular region of **glypican-1**, as therapeutic agent; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT 63551-76-8, Phosphoinositide-specific phospholipase C
RL: BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(**glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

IT 180766-04-5, GenBank AA046130
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT 535996-85-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed sequence; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)
IT 536003-39-1 536003-40-4 536003-41-5 536003-42-6 536003-43-7 536003-44-8 536003-45-9 536003-46-0
RL: PRP (Properties)
(unclaimed sequence; **glypican-1** determination and modulation in human breast cancer diagnosis and treatment)

L12 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:964393 CAPLUS
DOCUMENT NUMBER: 138:33702
TITLE: Proteins supporting proliferation or survival of hematopoietic stem cells and hematopoietic progenitor cells and a cDNA encoding it and their uses
INVENTOR(S): Nishikawa, Mitsuo; Drmanac, Radoje T.; Labat, Ivan; Lee, Juhi; Tang, Y. Tom; Stache-Crain, Birgit
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002100898	A2	20021219	WO 2002-JP5807		20020611
WO 2002100898	A3	20030530			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2449259	AA	20021219	CA 2002-2449259		20020611
EP 1395610	A2	20040310	EP 2002-733478		20020611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2005507240	T2	20050317	JP 2003-503664		20020611
US 2004220396	A1	20041104	US 2004-478926		20040617
PRIORITY APPLN. INFO.:			US 2001-297286P	P	20010611
			WO 2002-JP5807	W	20020611

ED Entered STN: 20 Dec 2002
AB Genes encoding proteins SCR-2 to SCR-8, that support proliferation or survival of hematopoietic stem cells or hematopoietic progenitor cells are identified. The genes were identified by comparing patterns of gene expression between cells which support proliferation or survival of hematopoietic stem cells or hematopoietic progenitor cells and cells which

do not support the proliferation or survival. Proliferation or survival of hematopoietic stem cells or hematopoietic progenitor cells is supported by using stromal cells in which the isolated gene is expressed or a gene product of the isolated gene. The mouse SCR-2 protein is almost identical to **glypican 1** and SCR-3 is a chemokine homolog. Expression of the cloned SCR-2 gene from a strong promoter in stromal cells resulted in increased proliferation of co-cultured hematopoietic stem cells.

IC ICM C07K014-475
ICS C12N015-12; C12N005-06; A61K038-00; C07K016-22

CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3, 15

IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**glypican 1**, sequence homolog; proteins supporting proliferation or survival of hematopoietic stem cells and hematopoietic progenitor cells and cDNA encoding it and their uses)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal, to hematopoiesis-supporting proteins; proteins supporting proliferation or survival of hematopoietic stem cells and hematopoietic progenitor cells and cDNA encoding it and their uses)

L12 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:937303 CAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2002355079	A2	20021210	JP 2002-69354		20020313
PRIORITY APPLN. INFO.:			JP 2001-73183	A	20010314
			JP 2001-74993	A	20010315
			JP 2001-102519	A	20010330

ED Entered STN: 10 Dec 2002

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

IC ICM C12N015-09

ICS C12N015-09; C12Q001-02; C12Q001-68; G01N033-53; G01N037-00
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 2, 4, 5, 9, 13
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1, DR1-associated protein 1 (neg. cofactor 2 α) 1;
endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD81 antigen (target of antiproliferative **antibody** 1);
endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)
IT **Proteins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DBY; endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genes)
IT **G** proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G protein sara; endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genes)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Ig superfamily containing leucine-rich repeat; endocrine disruptor
screening using DNA chips of endocrine disruptor-responsive genes)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**glypican-1**; endocrine disruptor screening using
DNA chips of endocrine disruptor-responsive genes)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(high affinity Ig ε receptor β subunit; endocrine
disruptor screening using DNA chips of endocrine disruptor-responsive
genes)
IT **Antibodies** and Immunoglobulins
(hypogammaglobulinemia, Bruton agammaglobulinemia tyrosine kinase;
endocrine disruptor screening using DNA chips of endocrine
disruptor-responsive genes)

L12 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:465423 CAPLUS
DOCUMENT NUMBER: 137:228256
TITLE: Human secretory signal peptide description by hidden Markov model and generation of a strong artificial signal peptide for secreted protein expression
AUTHOR(S): Barash, Steve; Wang, Wei; Shi, Yanggu
CORPORATE SOURCE: Department of Information Technology, Human Genome Sciences, Inc., Rockville, MD, 20850, USA
SOURCE: Biochemical and Biophysical Research Communications (2002), 294(4), 835-842
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Jun 2002
AB A hidden Markov model (HMM) has been used to describe, predict, identify, and generate secretory signal peptide sequences. The relative strengths of artificial secretory signals emitted from the human signal peptide HMM (SP-HMM) correlate with their HMM bit scores as determined by their effectiveness to direct alkaline phosphatase secretion. The nature of the

signal strength is in effect the closeness to the consensus. The HMM bit score of 8 is exptl. determined to be the threshold for discriminating signal sequences from non-secretory ones. An artificial SP-HMM generated signal sequence of the maximum model bit score (HMM +38) was selected as an ideal human signal sequence. This signal peptide (secrecon) directs strong protein secretion and expression. We further ranked the signal strengths of the signal peptides of the known human secretory proteins by SP-HMM bit scores. The applications of high-bit scoring HMM signals in recombinant protein production and protein engineering are discussed.

CC 6-3 (General Biochemistry)
Section cross-reference(s): 13

IT Proteins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**glypican-1**; human signal peptide hidden Markov model bit scores permit ranking of signal peptides from natural secreted protein precursors)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(heavy chain; human signal peptide hidden Markov model bit scores permit ranking of signal peptides from natural secreted protein precursors)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(λ chain V region (4A); human signal peptide hidden Markov model bit scores permit ranking of signal peptides from natural secreted protein precursors)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:618209 CAPLUS
DOCUMENT NUMBER: 135:193985
TITLE: Genes expressed in tumor cells and their use as diagnostic markers and the assessment of tumors to chemotherapy
INVENTOR(S): Roth, Frederick P.; Van Huffel, Christophe; White, James V.; Shyjan, Andrew W.
PATENT ASSIGNEE(S): Millennium Predictive Medicine, Inc., USA
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001061050	A2	20010823	WO 2001-US5301	20010216
WO 2001061050	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002120004	A1	20020829	US 2001-788099	20010216
US 2003129629	A1	20030710	US 2002-272111	20021016
PRIORITY APPLN. INFO.:			US 2000-183265P	P 20000217
			US 2001-788099	A1 20010216

ED Entered STN: 24 Aug 2001

AB The present invention is directed to the identification of markers that can be used to determine the sensitivity of cancer cells to a therapeutic agent. The present invention is also directed to the identification of therapeutic targets. Nucleic acid arrays were used to determine the level of expression of sequences (genes) found in 60 different solid tumor cancer cell lines selected from the NCI 60 cancer cell line series. Expression anal. was used to identify markers associated with sensitivity to certain chemotherapeutic agents.

IC ICM C12Q001-68

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 3

IT **Antibodies**
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to tumor markers; genes expressed in tumor cells and their use as diagnostic markers and assessment of tumors to chemotherapy)

IT 89338-42-1, Antigen HLA-DR (human clone pγ-2 γ-chain protein moiety) 96511-49-8 97599-20-7, Interleukin 1β (human clone pIL-1-14 precursor reduced) 98616-16-1, Protein CRBP (human clone 1 precursor reduced) 106908-71-8 107371-61-9 109656-69-1, Tropomyosin (human fibroblast clone 1401/32 reduced) 111237-10-6, Lipocortin PP 4 (human clone λHPAP1.6/λHPAP1.5 precursor) 114514-06-6, Protein (mouse clone F9-104/F9-12/C3H-82 guanine nucleotide-binding gene ypt1 reduced) 115471-18-6 117537-97-0, Plasmin (human clone pPI41/pPI39/pPI142 α2-inhibitor precursor protein moiety reduced) 118232-88-5 118549-55-6, Myosin (human clone hMLC-3 light chain 3) 121631-78-5 124544-53-2, Protein (human gene L-MYC2 reduced) 125008-34-6 126236-73-5, Glycophosphoprotein P (human clone pSVB1/pSVM113/pSVC6/pSVA4/pSVS13/pSVTH21 gene mdr1 protein moiety reduced) 126466-51-1, Antigen E 2 (human clone BC1 precursor protein moiety) 127188-11-8 128283-40-9 128284-97-9 128512-93-6 130704-09-5, Protein (human clone 5F/A4 20.5-kilodalton cysteine-rich reduced) 131715-68-9, Fibulin C (human precursor protein moiety reduced) **131753-81-6** 133402-03-6 133423-89-9, Cofilin (human placenta protein moiety reduced) 133925-44-7, Antigen CD 53 (human protein moiety reduced) 133925-94-7, Protein S 3 (human clone p54-2 ribosome reduced) 134089-75-1, Sialoglycoprotein VCAM 1b (human clone 1E11 precursor protein moiety reduced) 134116-73-7, Laminin (human clone C43/T3/E1/E61/D6/F8/E34/J4 B2-subunit precursor protein moiety reduced) 134944-20-0, RNA formation factor TCF 1 (human clone pRIT2-TCF-1C isoform C reduced) 135844-47-2, Antigen SP 100 (human clone Li-A/Li-B protein moiety reduced) 136253-20-8, Protein (human norepinephrine-transporting reduced) 137468-59-8, Lectin CBP 35 (human ZR-75-1 cell protein moiety) 137497-37-1, Midkine (human clone hMK-1 precursor reduced) 138363-41-4 138756-60-2, Antigen CD 9 (human clone λF-5 precursor protein moiety reduced) 139317-02-5, Protein CRABP-II (human clone λf1.1 reduced) 139568-91-5, Connective tissue growth factor (human clone DB60R32 precursor protein moiety reduced) 141176-86-5, Protein G (human clone 19A/5B/22H guanine nucleotide-binding α16-subunit reduced) 143298-35-5 143640-16-8, Integrin (human clone 3.410/3.285/3.24 α3-subunit precursor protein moiety reduced) 144131-77-1, Moesin (human clone UIII reduced) 144132-38-7, Antigen HLA-DM (human clone RING7 β-chain precursor reduced) 144416-02-4 144813-70-7, Protein S 25 (human clone PC.R8 ribosome) 145173-13-3 146044-99-7, RNA

formation factor RAP 30 (human) 146046-81-3, Intestinal trefoil factor (human clone HuPCR-ITF precursor reduced) 146151-12-4, Protein P 2 (human clone A2h myelin basic precursor reduced) 146704-87-2 146989-82-4, Protein IRF (human clone λIRF2/λIRF4 iron regulatory factor reduced) 147204-30-6 147278-56-6, Protein E1A-F (human clone pCDE1A-F/15'2-1 human adenovirus E1A enhancer-binding C-terminal fragment reduced) 147387-99-3 147571-82-2 147573-63-5 147603-70-1, Restin (human reduced) 147785-74-8, RNA formation factor ISGF-3 (human clone 38/48 interferon-stimulated γ-subunit reduced) 147855-41-2, RNA formation factor PSF (human clone A isoform reduced) 148264-49-7 148412-71-9, Protein MCP (human U937 cell macrophage capping deblocked reduced) 148591-61-1, Keratin 2 (human clone pEK2 reduced) 148641-23-0, Protein (human clone T47f36.52/U21C8B gene EMS1 reduced) 148996-73-0, Protein (human clone pART4 actin-related reduced) 149025-17-2 149371-69-7 149592-54-1 150226-92-9, Protein (human clone pAS2 gene CIP1 Cdk-interacting reduced) 150287-67-5 150475-48-2 150475-68-6, Protein (human gene SCN1B sodium channel-forming β1-subunit reduced) 150875-21-1 150951-35-2 151185-93-2, Protein p 48 (human clone RbAp48 retinoblastoma-binding reduced) 151381-65-6 151596-68-8 151688-76-5, Protein P1.B (human secretory precursor reduced) 151912-19-5 152744-64-4 152890-13-6 152990-73-3, Protein Shb (human reduced) 152990-86-8 153551-11-2 153701-86-1 154338-70-2 154571-10-5 155077-97-7 155078-14-1 155981-08-1 157297-82-0 157298-15-2 157908-58-2 157908-71-9 158652-74-5 158709-33-2 158935-67-2 158969-04-1 159521-57-0, Protein (human clone L4 gene DAN) 159521-93-4 159575-35-6 159966-15-1 160405-18-5 160405-30-1 160405-33-4 161350-52-3 161446-00-0, Cytokine 4-1BB ligand (human) 161629-56-7 161629-78-3 161631-09-0 161631-48-7 161706-40-7 161736-51-2, Protein p 33 (human) 161736-53-4 162077-36-3 162077-58-9 162242-60-6, Antigen (human clone MZ2 gene MAGE-11) 164205-93-0, Integrin (human α8 subunit precursor) 164639-39-8, Protein (human KG-1 cell 740-amino acid) 165945-21-1, Paxillin (human clone Pax-4) 167362-02-9, Protein S 9 (human ribosome) 167974-60-9, Protein (human clone F-T03796 gene STM2) 169239-28-5 169241-12-7 170973-06-5 170979-97-2 171263-71-1 171343-74-1 171601-28-8 172279-35-5 172279-45-7 172450-68-9 173014-66-9, Protein (human gene DD96) 175960-61-9 178465-55-9 183972-11-4 186208-13-9, Calpain (human) 205396-29-8 220128-76-7 221221-66-5 251922-64-2 256634-35-2 340767-26-2 349711-33-7 352053-22-6, Oxysterol binding protein 1 (human) 355485-55-1 355485-56-2 355485-57-3, Protein (human gene IFNA) 355485-58-4 355485-59-5 355485-60-8, Autoantigen p542 (human clone p542) 355485-61-9 355485-62-0, Vinculin (human gene VCL) 355485-63-1, Protein (human gene ITGB5) 355485-64-2 355485-65-3, Protein (human isolate LJ gene NK4) 355485-66-4 355485-67-5 355485-68-6, GS2NA (human cell line Hep G2) 355485-69-7 355485-70-0, Alpha (2) chain (human clone HD3, HD4) 355485-71-1 355485-72-2 355485-73-3 355485-74-4 355485-75-5 355485-76-6 355485-77-7, Tyrosine kinase (human gene RON) 355485-78-8 355485-79-9 355485-80-2 355485-81-3 355485-82-4, Tropomyosin (human WI-38 cell isoform) 355804-56-7 355804-61-4 355884-28-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes expressed in tumor cells and their use as diagnostic markers and assessment of tumors to chemotherapy)

L12 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:277880 CAPLUS
DOCUMENT NUMBER: 132:305482
TITLE: Glypicans for the detection and treatment of human

carcinoma
INVENTOR(S): Lander, Arthur; Korc, Murray
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000023109	A1	20000427	WO 1999-US24176		19991015
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2346264	AA	20000427	CA 1999-2346264		19991015
EP 1146903	A1	20011024	EP 1999-954963		19991015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AU 769125	B2	20040115	AU 2000-11181		19991015
US 2003103980	A1	20030605	US 2002-210327		20020731
PRIORITY APPLN. INFO.:			US 1998-104510P	P	19981016
			US 1999-121624P	P	19990225
			WO 1999-US24176	W	19991015
			US 2001-807575	A2	20010712
			US 2001-309722P	P	20010731

ED Entered STN: 28 Apr 2000
AB Glycosylphosphatidylinositol- (GPI-) anchored HSPG **glypican-1** is strongly expressed in human breast and pancreatic cancer - both by the cancer cells and in the case of pancreatic cancer the adjacent fibroblasts - whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast cancer tissues as well as breast cancer cells by comparison with breast normal tissues. Temporary or permanent transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EFG. Glypican can be used to detect the carcinoma in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of **glypican-1** are effective in retarding the growth of glypican-responsive carcinomas.
IC ICM A61K039-395
ICS C07K016-00; C12Q001-00; G01N033-53; G01N033-567; G01N033-574
CC 9-16 (Biochemical Methods)

Section cross-reference(s): 1, 2, 3, 7, 14
IT Animal tissue
Antitumor agents
Blood analysis
Body fluid
Carcinoma
Diagnosis
Gene therapy
Imaging
Immunoassay
Immunotherapy
Molecular cloning
Pancreas, neoplasm
(glypicans for detection and treatment of human carcinoma)
IT Nucleotides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(suppressing the expression of the extracellular region of **glypican 1**; glypicans for detection and treatment of human carcinoma)
IT **131753-81-6**, **Glypican 1**, human
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(glypicans for detection and treatment of human carcinoma)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:487381 CAPLUS
DOCUMENT NUMBER: 131:126414
TITLE: New members of the glypican gene family and the association of mutations with Simpson-Golabi-Behmel overgrowth syndrome
INVENTOR(S): Veugelers, Mark Paul Dittmar; David, Guido Joseph Frans
PATENT ASSIGNEE(S): Vlaams Interuniversitair Instituut Voor Biotechnologie, Belg.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9937764	A2	19990729	WO 1999-EP329		19990120
WO 9937764	A3	20000203			
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9924229	A1	19990809	AU 1999-24229		19990120
PRIORITY APPLN. INFO.:			EP 1998-200226	A	19980127
			WO 1999-EP329	W	19990120

ED Entered STN: 06 Aug 1999
AB The invention relates to a novel polynucleotide encoding a new glypican-related protein (glypican-6) and the gene for glypican-4 as well as derivs. of both genes for use in methods of diagnosis and therapy. Derivs. comprise for example fragments of the gene either isolated or synthetic and having a length that is smaller than the complete gene; primers, comprising ≥10 consecutive gene specific nucleotides, preferably about 20 gene specific consecutive nucleotides of the nucleotide sequence of the gene; longer oligonucleotides up to the full length of the gene; antisense variants of the gene, the fragments or the primers; antibodies directed to the gene, fragments, primers or complementary strands thereof; any specific ligand for DNA that can be used as a specific probe, peptide nucleic acid probes. Glypican-6 and glypican-4 are heparan sulfate proteoglycans 555 and 556 amino acid residues in length, resp. Their genes are localized to human chromosome 13q32 and Xq26, resp. Mutations in these genes and gene products are associated with Simpson-Golabi-Behmel overgrowth syndrome, and thus provide reagents for use in diagnosis or therapy. PCR primers/hybridization probes are provided for detecting mutations and/or translocations in the glypican genes, and antibodies may be used in immunoassays.
IC ICM C12N015-12
ICS C07K014-47; C07K014-475; G01N033-68; C12Q001-68; A61K031-70; A61K038-17
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 13, 14, 63
IT Proteoglycans, biological studies
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(heparitin sulfate-containing, **glypican-1**; members of the glypican gene family and the association of mutations with Simpson-Golabi-Behmel overgrowth syndrome)
IT **Antibodies**
Probes (nucleic acid)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(members of the glypican gene family and the association of mutations with Simpson-Golabi-Behmel overgrowth syndrome)
IT **131753-81-6** 187889-31-2, GenBank U66033-derived protein GI 1864085 218618-72-5, GenBank AF030186-derived protein GI 3831547 233272-65-6, Glypican 6 (human)
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; members of the glypican gene family and the association of mutations with Simpson-Golabi-Behmel overgrowth syndrome)

=> fil cancerlit biosis medline embase
FILE 'CANCERLIT' ENTERED AT 15:21:48 ON 12 SEP 2005

FILE 'BIOSIS' ENTERED AT 15:21:48 ON 12 SEP 2005

FILE 'MEDLINE' ENTERED AT 15:21:48 ON 12 SEP 2005

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FILE 'EMBASE' ENTERED AT 15:21:48 ON 12 SEP 2005
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=> d que l33
L3          109 SEA FILE=CAPLUS ABB=ON  PLU=ON  (GLYPICAN (2W) 1)/BI
L4         1550 SEA FILE=CAPLUS ABB=ON  PLU=ON  HEPAR!N/OBI(3A) SULFATE/OBI(3A)
                 PROTEOGLYCAN#/OBI
L13         259 SEA L3
L14        9855 SEA L4
L15         127 SEA L14 (L) GLYCOSYLPHOSPHATIDYLINO?
L16         354 SEA L13 OR L15
L19      626863 SEA ANTINEOPLAS? OR ANTITUMOR? OR ANTICANCER? OR ANTICARCINO?
L22     4460830 SEA CANCER? OR TUMOR? OR NEOPLAS? OR CARCINOM? OR NEOPLAS?
L25      508627 SEA BINDING (2W) (MOLECULE OR PROTEIN#)
L26          34 SEA L25 AND L16
L27           4 SEA L26 AND (L19 OR L22)
L28          34 SEA L27 OR L26
L29          16 DUP REM L28 (18 DUPLICATES REMOVED)
L30          13 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GLYPICAN (2W) 1
L31          12 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 (L) GLYCOSYLPHOSPHATIDYL
                INO?
L32          18 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L31 OR L30
L33          33 DUP REM L32 L29 (1 DUPLICATE REMOVED)


=> d bib ab ct l33 1-33

L33  ANSWER 1 OF 33  CANCERLIT on STN                    DUPLICATE 1
AN   1999433578     CANCERLIT
DN   99433578   PubMed ID: 10505759
TI   Stable transfection of a glypican-1 antisense
     construct decreases tumorigenicity in PANC-1 pancreatic carcinoma cells.
AU   Kleeff J; Wildi S; Kumbasar A; Friess H; Lander A D; Korc M
CS   Department of Medicine, University of California, Irvine 92697, USA.
NC   CA-40162 (NCI)
SO   PANCREAS, (1999 Oct) 19 (3) 281-8.
     Journal code: 8608542. ISSN: 0885-3177.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   MEDLINE; Priority Journals
OS   MEDLINE 1999433578
EM   199911
ED   Entered STN: 20000221
     Last Updated on STN: 20000221
AB   Glypican-1 belongs to a family of
     glycosylphosphatidylinositol (GPI)-anchored heparan
     sulfate proteoglycans (HSPGs) that affect cell growth,
     invasion, and adhesion. Cell-surface HSPGs are believed to act as
     co-receptors for heparin-binding mitogenic growth factors. It was reported
     that glypican-1 is strongly expressed in human
     pancreatic cancer, and that it may play an essential role in regulating
     growth-factor responsiveness in pancreatic carcinoma cells. In this study
     we investigated the effects of decreased glypican-1
     expression in PANC-1 pancreatic cancer cells. To this end, PANC-1 cells
     were stable transfected with a full-length glypican-1
     antisense construct. The glypican- antisense transfected clones displayed
     markedly reduced glypican- protein levels and a marked attenuation of the
     mitogenic responses to heparin-binding growth factors that are commonly
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overexpressed in pancreatic cancer: fibroblast growth factor-2 (FGF2), heparin-binding epidermal growth factor (EGF)-like growth factor (HB-EGF), and hepatocyte growth factor (HGF). In addition, **glypican-1** antisense-expressing PANC-1 cells exhibited a significantly reduced ability to form tumors in nude mice in comparison with parental and sham-transfected PANC-1 cells. These data suggest that **glypican-1** plays an important role in the responses of pancreatic cancer cells to heparin-binding growth factors, and documents for the first time that its expression may enhance tumorigenic potential in vivo.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Carcinoma: GE, genetics
*Carcinoma: ME, metabolism
Carcinoma: PA, pathology
Cell Division: DE, drug effects
DNA, Antisense: BI, biosynthesis
*DNA, Antisense: PD, pharmacology
Dose-Response Relationship, Drug
Gene Expression: DE, drug effects
Growth Substances: GE, genetics
Growth Substances: PD, pharmacology
Heparan Sulfate Proteoglycan: BI, biosynthesis
*Heparan Sulfate Proteoglycan: GE, genetics
Mice
Mice, Nude
Neoplasm Transplantation
Pancreatic Neoplasms: GE, genetics
*Pancreatic Neoplasms: ME, metabolism
Pancreatic Neoplasms: PA, pathology
Polysaccharide-Lyases: ME, metabolism
RNA, Antisense: BI, biosynthesis
RNA, Messenger: BI, biosynthesis
RNA, Messenger: PD, pharmacology
Transfection
Tumor Cells, Cultured

L33 ANSWER 2 OF 33 CANCERLIT on STN
AN 2002195882 CANCERLIT
DN 22194352 PubMed ID: 12084716
TI Copper-dependent autocleavage of **glypican-1** heparan sulfate by nitric oxide derived from intrinsic nitrosothiols.
AU Ding Kan; Mani Katrin; Cheng Fang; Belting Mattias; Fransson Lars-Ake
CS Department of Cell and Molecular Biology, Section for Cell and Matrix Biology, Lund University, BMC C13, SE-221 84, Lund, Sweden.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Sep 6) 277 (36) 33353-60. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2002448141
EM 200210
ED Entered STN: 20021115
Last Updated on STN: 20021115
AB Cell surface heparan sulfate proteoglycans facilitate uptake of growth-promoting polyamines (Belting, M., Borsig, L., Fuster, M. M., Brown, J. R., Persson, L., Fransson, L.-A., and Esko, J. D. (2002) Proc. Natl. Acad. Sci. U. S. A. 99, 371-376). Increased polyamine uptake correlates with an increased number of positively charged N-unsubstituted

glucosamine units in the otherwise polyanionic heparan sulfate chains of **glypican-1**. During intracellular recycling of **glypican-1**, there is an NO-dependent deaminative cleavage of heparan sulfate at these glucosamine units, which would eliminate the positive charges (Ding, K., Sandgren, S., Mani, K., Belting, M., and Fransson, L.-A. (2001) J. Biol. Chemical 276, 46779-46791). Here, using both biochemical and microscopic techniques, we have identified and isolated S-nitrosylated forms of **glypican-1** as well as slightly charged **glypican-1** glycoforms containing heparan sulfate chains rich in N-unsubstituted glucosamines. These glycoforms were converted to highly charged species upon treatment of cells with 1 mm l-ascorbate, which releases NO from nitrosothiols, resulting in deaminative cleavage of heparan sulfate at the N-unsubstituted glucosamines. S-Nitrosylation and subsequent deaminative cleavage were abrogated by inhibition of a Cu(2+)/Cu(+) redox cycle. Under cell-free conditions, purified S-nitrosylated **glypican-1** was able to autocleave its heparan sulfate chains when NO release was triggered by l-ascorbate. The heparan sulfate fragments generated in cells during this autocatalytic process contained terminal anhydromannose residues. We conclude that the core protein of **glypican-1** can slowly accumulate NO as nitrosothiols, whereas Cu(2+) is reduced to Cu(+). Subsequent release of NO results in efficient deaminative cleavage of the heparan sulfate chains attached to the same core protein, whereas Cu(+) is oxidized to Cu(2+).

CT Check Tags: Human; Support, Non-U.S. Gov't
Catalysis
Cell-Free System
Chromatography, High Pressure Liquid
Copper: ME, metabolism
*Copper: PD, pharmacology
Heparan Sulfate Proteoglycan: CH, chemistry
*Heparan Sulfate Proteoglycan: ME, metabolism
Ions
Microscopy, Confocal
Microscopy, Fluorescence
Models, Biological
*Nitric Oxide: ME, metabolism
Protein Isoforms: ME, metabolism
Protein Structure, Tertiary
*S-Nitrosothiols: ME, metabolism
Tumor Cells, Cultured
Up-Regulation

L33 ANSWER 3 OF 33 CANCERLIT on STN
AN 2002195884 CANCERLIT
DN 22194354 PubMed ID: 12084721
TI FGF3 attached to a phosholipid membrane anchor gains a high transforming capacity. Implications of microdomains for FGF3 cell transformation.
AU Kohl Roman; Antoine Marianne; Reimers Kerstin; Kiefer Paul
CS Heinrich-Heine-Universitat, Medizinische Fakultat, Institut fur Hamostaseologie und Transfusionsmedizin, Moorenstrabetae 5, D-Dusseldorf, Germany.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Sep 6) 277 (36) 32760-7. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2002448088
EM 200210

ED Entered STN: 20021115
Last Updated on STN: 20021115

AB NIH3T3 cells transformed by mouse FGF3-cDNA (DMI cells) selected for their ability to grow as anchorage-independent colonies in soft agar and in defined medium lacking growth factors exhibit a highly transformed phenotype. We have used dominant negative (DN) fibroblast growth factor (FGF) receptor 2 (FGFR2) isoforms to block the FGF response in DMI cells. When the DN-FGFR was expressed in DMI cells, their transformed phenotype can be reverted. The truncated FGFR2(IIIb), the high affinity FGFR for FGF3, is significantly more efficient at reverting the transformed phenotype as the IIIc isoform, reaffirming the notion that the affinity of the ligand to the DN-FGFR2 isoform determines the effect. Heparin or heparan sulfate displaces FGF3 from binding sites on the cell surface inhibiting the growth of DMI cells and reverts the transformed phenotype (). However, the presence of heparin is necessary to induce a mitogenic response in NIH3T3 cells when stimulated with soluble purified mouse FGF3. We have investigated the importance of cell surface binding of FGF3 for its ability to transform NIH3T3 cells by creating an FGF3 mutant anchored to the membrane via **glycosylphosphatidylinositol** (GPI). The GPI anchor renders the cell surface association of FGF3 independent from binding to **heparan sulfate-proteoglycan** of the cell surface membrane. Attachment of a GPI anchor to FGF3 also confers a much higher transforming potential to the growth factor. Even more, the purified GPI-attached FGF3 is as much transforming as the secreted protein acting in an autocrine mode. Because NIH3T3 cells do not express the high affinity tyrosine kinase FGF receptors for FGF3, these findings suggest that FGF3 attached to GPI-linked **heparan sulfate-proteoglycan** may have a broader biological activity as when bound to transmembrane or soluble **heparan sulfate-proteoglycan.**

CT Check Tags: Animal
3T3 Cells
Amino Acid Sequence
Blotting, Northern
COS Cells
Cell Line
Cell Membrane: ME, metabolism
Fibroblast Growth Factors: CH, chemistry
*Fibroblast Growth Factors: ME, metabolism
*Fibroblast Growth Factors: PH, physiology
Fibroblasts: ME, metabolism
Genes, Dominant
Heparin: PD, pharmacology
Heparitin Sulfate: PD, pharmacology
Immunoblotting
Iodine: ME, metabolism
Lactoperoxidase: ME, metabolism
Ligands
Mice
Microscopy, Fluorescence
Mitogens: ME, metabolism
Molecular Sequence Data
Mutation
*Phospholipids: ME, metabolism
Plasmids: ME, metabolism
Precipitin Tests
Protein Binding
Protein Isoforms
Protein Structure, Tertiary
Proto-Oncogene Protein p21(ras): ME, metabolism

Proto-Oncogene Proteins: CH, chemistry
*Proto-Oncogene Proteins: ME, metabolism
*Proto-Oncogene Proteins: PH, physiology
Transfection

L33 ANSWER 4 OF 33 CANCERLIT on STN
AN 2002149856 CANCERLIT
DN 21995860 PubMed ID: 12000726
TI Characterization of gene expression profiles in intraductal papillary-mucinous tumors of the pancreas.
AU Terris Benoit; Blaveri Ekaterina; Crnogorac-Jurcevic Tatjana; Jones Melanie; Missiaglia Edoardo; Ruszniewski Philippe; Sauvanet Alain; Lemoine Nicholas R
CS Cancer Research UK Molecular Oncology Unit, Imperial College School of Medicine at Hammersmith Campus, London, United Kingdom.
SO AMERICAN JOURNAL OF PATHOLOGY, (2002 May) 160 (5) 1745-54.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Abridged Index Medicus Journals; Priority Journals
OS MEDLINE 2002261006
EM 200206
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB The molecular pathology of precursor lesions leading to invasive pancreatic ductal adenocarcinomas remains relatively unknown. We have applied cDNA microarray analysis to characterize gene expression profiles in a series of intraductal papillary-mucinous tumors (IPMTs) of the pancreas, which represents one of the alternative routes of intraepithelial progression to full malignancy in the pancreatic duct system. Using a cDNA microarray containing 4992 human genes, we screened a total of 13 IPMTs including nine noninvasive and four invasive cases. Expression change in more than half of the tumors was observed for 120 genes, ie, 62 up-regulated and 58 down-regulated genes. Some of the up-regulated genes in this study have been previously described in classical pancreatic carcinomas such as lipocalin 2, galectin 3, claudin 4, and cathepsin E. The most highly up-regulated genes in IPMTs corresponded to three members of the trefoil factor family (TFF1, TFF2, and TFF3). Immunohistochemistry performed on five genes found to be differentially expressed at the RNA level (TFF1, TFF2, TFF3, lipocalin 2, and galectin 3) showed a good concordance between transcript level and protein abundance, except for TFF2. Hierarchical clustering organized the cases according to the dysplastic and invasive phenotype of theIPMTs. This analysis has permitted us to implicate several genes (caveolin 1, **glypican 1**, growth arrest-specific 6 protein, cysteine-rich angiogenic inducer 61) in tumor progression. The observation that several genes are differentially expressed both in IPMTs and pancreatic carcinomas suggests that they may be involved at an early stage of pancreatic carcinogenesis.
CT Check Tags: Human
Adenocarcinoma, Mucinous: GE, genetics
*Adenocarcinoma, Mucinous: PA, pathology
Bile Ducts, Intrahepatic: ME, metabolism
*Bile Ducts, Intrahepatic: PA, pathology
Carcinoma, Papillary: GE, genetics
*Carcinoma, Papillary: PA, pathology
Cell Line, Transformed
*Gene Expression Profiling
Oligonucleotide Array Sequence Analysis

Pancreas: ME, metabolism
Pancreas: PA, pathology
Pancreatic Neoplasms: GE, genetics
*Pancreatic Neoplasms: PA, pathology
RNA, Neoplasm: GE, genetics
RNA, Neoplasm: ME, metabolism

L33 ANSWER 5 OF 33 CANCERLIT on STN
AN 2002051546 CANCERLIT
DN 21269287 PubMed ID: 11106655
TI Mechanisms underlying preferential assembly of heparan sulfate on **glypican-1.**
AU Chen R L; Lander A D
CS Department of Developmental and Cell Biology and Developmental Biology Center, University of California, Irvine 92697, USA.
NC NS26862 (NINDS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Mar 9) 276 (10) 7507-17. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2001290815
EM 200107
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB Glypicans are major cell surface **heparan sulfate proteoglycans**, the structures of which are characterized by the presence of a cysteine-rich globular domain, a short glycosaminoglycan (GAG) attachment region, and a **glycosylphosphatidylinositol** membrane anchor. Despite strong evolutionary conservation of the globular domains of glypicans, no function has yet been attributed to them. By using a novel quantitative approach for assessing proteoglycan glycosylation, we show here that removal of the globular domain from rat **glypican-1** converts the proteoglycan from one that bears approximately 90% heparan sulfate (HS) to one that bears approximately 90% chondroitin sulfate. Mutational analysis shows that sequences at least 70 amino acids away from the **glypican-1** GAG attachment site are required for preferential HS assembly, although more nearby sequences also play a role. The effects of the **glypican-1** globular domain on HS assembly could also be demonstrated by fusing this domain to sequences representing the GAG attachment sites of other proteoglycans or, surprisingly, simply by expressing the isolated globular domain in cells and analyzing effects either on an exogenously expressed **glypican-1** GAG attachment domain or on endogenous proteoglycans. Quantitative analysis of the effect of the globular domain on GAG addition to proteoglycan core proteins suggested that preferential HS assembly is achieved, at least in part, through the inhibition of chondroitin sulfate assembly. These data identify the **glypican-1** globular domain as a structural motif that potently influences GAG class determination and suggest that an important role of glypican globular domains is to ensure a high level of HS substitution of these proteoglycans.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
CHO Cells
COS Cells
Cations
Chemiluminescence
Chondroitin Sulfates: CH, chemistry

Chondroitin Sulfates: ME, metabolism
DNA Mutational Analysis
Electrophoresis, Polyacrylamide Gel
Hamsters
*Heparan Sulfate Proteoglycan: CH, chemistry
*Heparitin Sulfate: ME, metabolism
Models, Biological
Molecular Sequence Data
Mutation
Plasmids: ME, metabolism
Protein Structure, Tertiary
Proteoglycans: ME, metabolism
Rats
Recombinant Fusion Proteins: CH, chemistry
Recombinant Fusion Proteins: ME, metabolism
Sequence Homology, Amino Acid
Transfection

L33 ANSWER 6 OF 33 CANCERLIT on STN
AN 2002067184 CANCERLIT
DN 21347237 PubMed ID: 11454708
TI **Glypican-1** is overexpressed in human breast cancer and modulates the mitogenic effects of multiple heparin-binding growth factors in breast cancer cells.
AU Matsuda K; Maruyama H; Guo F; Kleeff J; Itakura J; Matsumoto Y; Lander A D; Korc M
CS Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Biological Chemistry, and Pharmacology, University of California, Irvine, California 92697, USA.
NC CA-40162 (NCI)
NS-26862 (NINDS)
SO CANCER RESEARCH, (2001 Jul 15) 61 (14) 5562-9.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2001407894
EM 200108
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB Glypicans are a family of **glycosylphosphatidylinositol**-anchored cell surface **heparan sulfate proteoglycans** implicated in the control of cellular growth and differentiation. Here we show that **glypican-1** is strongly expressed in human breast cancers, whereas expression of **glypican-1** is low in normal breast tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in breast cancers by comparison with normal breast tissues, and glypican-2 and -5 are below the level of detection by Northern blotting in both normal and cancer samples. Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a **glypican-1** antisense construct markedly decreased **glypican-1** protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin alpha, heregulin beta, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both breast cancer tissues and breast cancer cells when compared with

normal breast tissues. There was a good correlation between **glypican-1** and syndecan-1 expression in the tumors. However, clones expressing the **glypican-1** antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 tumors with stage 2 or 3 disease exhibited high levels of **glypican-1** by Northern blot analysis. In contrast, low levels of **glypican-1** mRNA were evident in 1 of 10 tumors with stage 2 or 3 disease and in 9 of 10 tumors with stage 1 disease. Taken together, these data suggest that **glypican-1** may play a pivotal role in the ability of breast cancer cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Aged
Blotting, Northern
*Breast Neoplasms: GE, genetics
Breast Neoplasms: ME, metabolism
Breast Neoplasms: PA, pathology
DNA, Antisense: GE, genetics
Gene Expression Regulation, Neoplastic
*Growth Substances: PD, pharmacology
Heparan Sulfate Proteoglycan: AN, analysis
*Heparan Sulfate Proteoglycan: GE, genetics
Immunohistochemistry
In Situ Hybridization
Membrane Glycoproteins: AN, analysis
Membrane Glycoproteins: GE, genetics
Middle Age
Phospholipase C: ME, metabolism
Phospholipase C: PD, pharmacology
Proteoglycans: AN, analysis
Proteoglycans: GE, genetics
RNA, Messenger: GE, genetics
RNA, Messenger: ME, metabolism
Transfection
Tumor Cells, Cultured: DE, drug effects
Tumor Cells, Cultured: ME, metabolism

L33 ANSWER 7 OF 33 CANCERLIT on STN
AN 2002089450 CANCERLIT
DN 21525649 PubMed ID: 11669479
TI Cell-surface proteoglycan expression by lymphocytes from peripheral blood and gingiva in health and periodontal disease.
AU Manakil J F; Sugerman P B; Li H; Seymour G J; Bartold P M
CS School of Dentistry, The University of Queensland, Brisbane, Australia.
SO JOURNAL OF DENTAL RESEARCH, (2001 Aug) 80 (8) 1704-10.
Journal code: 0354343. ISSN: 0022-0345.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Dental Journals; Priority Journals
OS MEDLINE 2001566574
EM 200112
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB Cell-surface proteoglycans are involved in lymphocyte migration and

activation. This study investigated the expression of syndecan-1, syndecan-4, and glypican in peripheral blood lymphocytes and by lymphocytes in variously inflamed periodontal tissues. Gingival specimens from healthy, gingivitis, or chronic periodontitis sites were stained by means of antibodies against B- and T-lymphocytes and also syndecan-1, syndecan-4, and **glypican.** Syndecan-**1** expression by peripheral blood mononuclear cells (PBMC) from healthy, gingivitis, and chronic periodontitis subjects was assessed by flow cytometry. Syndecan-1 was expressed by B-cells/plasma cells but not T-cells in both gingivitis and chronic periodontitis lesions. Both B-cells/plasma cells and T-cells in gingivitis and chronic periodontitis expressed syndecan-4. Glypican was expressed only by macrophages. Stimulation of PBMC with mitogens and growth factors modulated syndecan-1 expression in both the T- and B-cells. Thus, cell-surface proteoglycan expression by lymphocytes in periodontal inflammation is cell-type-specific and may be modulated by inflammation.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Alveolar Bone Loss: ME, metabolism
Alveolar Bone Loss: PA, pathology
Analysis of Variance
B-Lymphocytes: ME, metabolism
B-Lymphocytes: PA, pathology
Chronic Disease
Flow Cytometry
Gingiva: ME, metabolism
*Gingiva: PA, pathology
Gingival Hemorrhage: ME, metabolism
Gingival Hemorrhage: PA, pathology
Gingivitis: BL, blood
Gingivitis: ME, metabolism
*Gingivitis: PA, pathology
Growth Substances: PD, pharmacology
*Heparan Sulfate Proteoglycan: AN, analysis
Lymphocytes: ME, metabolism
*Lymphocytes: PA, pathology
Macrophages: ME, metabolism
Macrophages: PA, pathology
*Membrane Glycoproteins: AN, analysis
Middle Age
Mitogens: PD, pharmacology
Periodontal Attachment Loss: ME, metabolism
Periodontal Attachment Loss: PA, pathology
Periodontal Pocket: ME, metabolism
Periodontal Pocket: PA, pathology
Periodontitis: BL, blood
Periodontitis: ME, metabolism
*Periodontitis: PA, pathology
Plasma Cells: ME, metabolism
Plasma Cells: PA, pathology
*Proteoglycans: AN, analysis
Regression Analysis
Statistics
T-Lymphocytes: ME, metabolism
T-Lymphocytes: PA, pathology
Tooth Cervix: PA, pathology

L33 ANSWER 8 OF 33 CANCERLIT on STN
AN 2000490844 CANCERLIT
DN 20490844 PubMed ID: 11034601

TI Regulation of cytokine signaling by B cell antigen receptor and CD40-controlled expression of heparan sulfate proteoglycans.
AU van der Voort R; Keehnen R M; Beuling E A; Spaargaren M; Pals S T
CS Department of Pathology, Academic Medical Center, University of Amsterdam, 1105 AZ Amsterdam, The Netherlands.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (2000 Oct 16) 192 (8) 1115-24.
Journal code: 2985109R. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2001021679
EM 200011
ED Entered STN: 20010423
Last Updated on STN: 20010423
AB Recently, biochemical, cell biological, and genetic studies have converged to reveal that integral membrane heparan sulfate proteoglycans (HSPGs) are critical regulators of growth and differentiation of epithelial and connective tissues. As a large number of cytokines involved in lymphoid tissue homeostasis or inflammation contain potential HS-binding domains, HSPGs presumably also play important roles in the regulation of the immune response. In this report, we explored the expression, regulation, and function of HSPGs on B lymphocytes. We demonstrate that activation of the B cell antigen receptor (BCR) and/or CD40 induces a strong transient expression of HSPGs on human tonsillar B cells. By means of these HSPGs, the activated B cells can bind hepatocyte growth factor (HGF), a cytokine that regulates integrin-mediated B cell adhesion and migration. This interaction with HGF is highly selective since the HSPGs did not bind the chemokine stromal cell-derived factor (SDF)-1 alpha, even though the affinities of HGF and SDF-1alpha for heparin are similar. On the activated B cells, we observed induction of a specific HSPG isoform of CD44 (CD44-HS), but not of other HSPGs such as syndecans or **glypican-1**. Interestingly, the expression of CD44-HS on B cells strongly promotes HGF-induced signaling, resulting in an HS-dependent enhanced phosphorylation of Met, the receptor tyrosine kinase for HGF, as well as downstream signaling molecules including Grb2-associated binder 1 (Gab1) and Akt/protein kinase B (PKB). Our results demonstrate that the BCR and CD40 control the expression of HSPGs, specifically CD44-HS. These HSPGs act as functional coreceptors that selectively promote cytokine signaling in B cells, suggesting a dynamic role for HSPGs in antigen-specific B cell differentiation.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Antigens, CD40: PH, physiology
Antigens, CD44: GE, genetics
Antigens, CD44: PH, physiology
B-Lymphocytes: IM, immunology
*B-Lymphocytes: PH, physiology
Burkitt Lymphoma
Cells, Cultured
Chemokines, CXC: PK, pharmacokinetics
Chemokines, CXC: PD, pharmacology
*Cytokines: PH, physiology
Fibroblast Growth Factor 2: PD, pharmacology
*Heparan Sulfate Proteoglycan: BI, biosynthesis
Hepatocyte Growth Factor: ME, metabolism
Kinetics
*Receptors, Antigen, B-Cell: IM, immunology
Signal Transduction: DE, drug effects
Signal Transduction: PH, physiology
Stromal Cells: PH, physiology

Tonsil: IM, immunology
Transfection
Tumor Cells, Cultured

L33 ANSWER 9 OF 33 CANCERLIT on STN
AN 2000062819 CANCERLIT
DN 20062819 PubMed ID: 10593896
TI Similarities and differences between the effects of heparin and **glypican-1** on the bioactivity of acidic fibroblast growth factor and the keratinocyte growth factor.
AU Berman B; Ostrovsky O; Shlissel M; Lang T; Regan D; Vlodavsky I; Ishai-Michaeli R; Ron D
CS Department of Biology, Technion-Israel Institute of Technology, Haifa 32000, Israel.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Dec 17) 274 (51) 36132-8. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2000062819
EM 200001
ED Entered STN: 20000221
Last Updated on STN: 20020726
AB The keratinocyte growth factor (KGF or FGF-7) is unique among its family members both in its target cell specificity and its inhibition by the addition of heparin and the native heparan-sulfate proteoglycan (HSPG), **glypican-1** in cells expressing endogenous HSPGs. FGF-1, which binds the FGF-7 receptor with a similar affinity as FGF-7, is stimulated by both molecules. In the present study, we investigated the modulation of FGF-7 activities by heparin and **glypican-1** in HS-free background utilizing either HS-deficient cells expressing the FGF-7 receptor (designated BaF/KGFR cells) or soluble extracellular domain of the receptor. At physiological concentrations of FGF-7, heparin was required for high affinity receptor binding and for signaling in BaF/KGFR cells. In contrast, binding of FGF-7 to the soluble form of the receptor did not require heparin. However, high concentrations of heparin inhibited the binding of FGF-7 to both the cell surface and the soluble receptor, similar to the reported effect of heparin in cells expressing endogenous HSPGs. The difference in heparin dependence for high affinity interaction between the cell surface and soluble receptor may be due to other molecule(s) present on cell surfaces. **Glypican-1** differed from heparin in that it stimulated FGF-1 but not FGF-7 activities in BaF/KGFR cells. **Glypican-1** abrogated the stimulatory effect of heparin, and heparin reversed the inhibitory effect of **glypican-1**, indicating that this HSPG inhibits FGF-7 activities by acting, most likely, as a competitive inhibitor of stimulatory HSPG species for FGF-7. The regulatory effect of **glypican-1** is mediated at the level of interaction with the growth factor as **glypican-1** did not bind the KGFR. The effect of heparin and **glypican-1** on FGF-1 and FGF-7 oligomerization was studied employing high and physiological concentrations of growth factors. We did not find a correlation between the effects of these glycosaminoglycans on FGFs biological activity and oligomerization. Altogether, our findings argue against the heparin-linked dimer presentation model as key in FGFR activation, and support the notion that HSPGs primarily affect high affinity interaction of FGFs with their receptors.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Line

Dimerization
*Fibrinolytic Agents: ME, metabolism
Fibrinolytic Agents: PD, pharmacology
*Fibroblast Growth Factor 1: ME, metabolism
*Growth Substances: ME, metabolism
*Heparan Sulfate Proteoglycan: ME, metabolism
Heparan Sulfate Proteoglycan: PD, pharmacology
*Heparin: ME, metabolism
Heparin: PD, pharmacology
Rats
Receptors, Fibroblast Growth Factor: ME, metabolism
Receptors, Growth Factor: ME, metabolism
Signal Transduction: DE, drug effects

L33 ANSWER 10 OF 33 CANCERLIT on STN
AN 1999445549 CANCERLIT
DN 99445549 PubMed ID: 10514475
TI Functional association of type IIA secretory phospholipase A(2) with the **glycosylphosphatidylinositol**-anchored **heparan sulfate proteoglycan** in the cyclooxygenase-2-mediated delayed prostanoid-biosynthetic pathway.
AU Murakami M; Kambe T; Shimbara S; Yamamoto S; Kuwata H; Kudo I
CS Department of Health Chemistry, School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Oct 15) 274 (42) 29927-36. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1999445549
EM 199911
ED Entered STN: 20000221
Last Updated on STN: 20000221
AB An emerging body of evidence suggests that type IIA secretory phospholipase A(2) (sPLA(2)-IIA) participates in the amplification of the stimulus-induced cyclooxygenase (COX)-2-dependent delayed prostaglandin (PG)-biosynthetic response in several cell types. However, the biological importance of the ability of sPLA(2)-IIA to bind to **heparan sulfate proteoglycan** (HSPG) on cell surfaces has remained controversial. Here we show that glypican, a **glycosylphosphatidylinositol** (GPI)-anchored HSPG, acts as a physical and functional adaptor for sPLA(2)-IIA. sPLA(2)-IIA-dependent PGE(2) generation by interleukin-1-stimulated cells was markedly attenuated by treatment of the cells with heparin, heparinase or GPI-specific phospholipase C, which solubilized the cell surface-associated sPLA(2)-IIA. Overexpression of **glypican-1** increased the association of sPLA(2)-IIA with the cell membrane, and **glypican-1** was coimmunoprecipitated by the antibody against sPLA(2)-IIA. **Glypican-1** overexpression led to marked augmentation of sPLA(2)-IIA-mediated arachidonic acid release, PGE(2) generation, and COX-2 induction in interleukin-1-stimulated cells, particularly when the sPLA(2)-IIA expression level was suboptimal. Immunofluorescent microscopic analyses of cytokine-stimulated cells revealed that sPLA(2)-IIA was present in the caveolae, a microdomain in which GPI-anchored proteins reside, and also appeared in the perinuclear area in proximity to COX-2. We therefore propose that a GPI-anchored HSPG glypican facilitates the trafficking of sPLA(2)-IIA into particular subcellular compartments, and arachidonic acid thus released from the compartments may link efficiently to the downstream

COX-2-mediated PG biosynthesis.
CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Line
*Dinoprostone: BI, biosynthesis
*Glycosylphosphatidylinositols: ME, metabolism
*Heparan Sulfate Proteoglycan: ME, metabolism
Interleukin-1: PD, pharmacology
*Isoenzymes: ME, metabolism
*Phospholipases A: ME, metabolism
*Prostaglandin-Endoperoxide Synthase: ME, metabolism
Protein Binding
Subcellular Fractions: EN, enzymology
Tumor Necrosis Factor: PD, pharmacology

L33 ANSWER 11 OF 33 CANCERLIT on STN
AN 1999214150 CANCERLIT
DN 99214150 PubMed ID: 10196157
TI **Glypican-1** is a VEGF165 binding proteoglycan that acts as an extracellular chaperone for VEGF165.
AU Gengrinovitch S; Berman B; David G; Witte L; Neufeld G; Ron D
CS Department of Biology, Technion-Israel Institute of Technology, Haifa 32000, Israel.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Apr 16) 274 (16) 10816-22.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1999214150
EM 199905
ED Entered STN: 19990622
Last Updated on STN: 19990622
AB **Glypican-1** is a member of a family of **glycosylphosphatidylinositol** anchored cell surface **heparan sulfate proteoglycans** implicated in the control of cellular growth and differentiation. The 165-amino acid form of vascular endothelial growth factor (VEGF165) is a mitogen for endothelial cells and a potent angiogenic factor in vivo. Heparin binds to VEGF165 and enhances its binding to VEGF receptors. However, native HSPGs that bind VEGF165 and modulate its receptor binding have not been identified. Among the **glypicans**, **glypican-1** is the only member that is expressed in the vascular system. We have therefore examined whether **glypican-1** can interact with VEGF165. **Glypican-1** from rat myoblasts binds specifically to VEGF165 but not to VEGF121. The binding has an apparent dissociation constant of 3 x 10(-10) M. The binding of **glypican-1** to VEGF165 is mediated by the heparan sulfate chains of **glypican-1**, because heparinase treatment abolishes this interaction. Only an excess of heparin or heparan sulfates but not other types of glycosaminoglycans inhibited this interaction. VEGF165 interacts specifically not only with rat myoblast **glypican-1** but also with human endothelial cell-derived **glypican-1.** The binding of 125I-VEGF165 to heparinase-treated human vascular endothelial cells is reduced following heparinase treatment, and addition of **glypican-1** restores the binding. **Glypican-1** also potentiates the binding of 125I-VEGF165 to a soluble extracellular domain of the VEGF receptor KDR/flk-1. Furthermore, we show that **glypican-1** acts as an extracellular chaperone that can restore the receptor binding ability of VEGF165, which has been damaged by oxidation. Taken together, these results suggest that **glypican-1**

may play an important role in the control of angiogenesis by regulating the activity of VEGF165, a regulation that may be critical under conditions such as wound repair, in which oxidizing agents that can impair the activity of VEGF are produced, and in situations were the concentrations of active VEGF are limiting.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Endothelial Growth Factors: ME, metabolism
*Lymphokines: ME, metabolism
Membrane Proteins: ME, metabolism
*Molecular Chaperones: ME, metabolism
Oxidation-Reduction
Protein Binding
*Proteoglycans: ME, metabolism
Recombinant Proteins: ME, metabolism

L33 ANSWER 12 OF 33 CANCERLIT on STN
AN 2000096947 CANCERLIT
DN 20096947 PubMed ID: 10629564
TI Expression pattern alterations of syndecans and **glypican-1** in normal and pathological trophoblast.
AU Crescimanno C; Marzioni D; Paradinas F J; Schrurs B; Muhlhauser J; Todros T; Newlands E; David G; Castellucci M
CS Institute of Anatomy and Histology, University of Verona, Italy.
SO JOURNAL OF PATHOLOGY, (1999 Dec) 189 (4) 600-8.
Journal code: 0204634. ISSN: 0022-3417.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2000096947
EM 200002
ED Entered STN: 20000314
Last Updated on STN: 20000314
AB Syndecans (syn-1, -2, -3, -4) and **glypican-1** are proteoglycans expressed during development in association with changes in tissue organization and differentiation. They participate in the modulation of growth factor actions and in cell-cell and cell-matrix adhesion. The expression of syn-1, -2, -3, -4, and **glypican-1** has been studied in normal human placenta and in gestational trophoblastic disease such as hydatidiform mole, invasive mole, and choriocarcinoma, using immunohistochemistry and western blots. Syndecan-3 was not expressed in normal or pathological tissues. During normal gestation, the other proteoglycans showed a specific staining pattern, which for some was modified during pregnancy. For instance, syn-1 was only expressed in syncytiotrophoblast; syn-4 was mainly localized in the villous and extravillous cytotrophoblast in the first trimester, whereas at term it was expressed in the syncytiotrophoblast. The most striking results are the altered expression patterns of syndecans and **glypican-1** in pathological tissues. These proteoglycans showed a progressive decrease of immunostaining related to the increase of severity of trophoblastic disease, in particular in invasive mole and choriocarcinoma. In addition, dysregulation in the localization of the expression patterns was observed for syn-2 and -4. Because changes in syndecan expression enable cells to become more or less responsive to their micro-environment, the down-regulation and/or dysregulation of syndecans in relation to the degree of severity of trophoblastic diseases provides new insights into the progression of these pathologies.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Blotting, Western

Choriocarcinoma: ME, metabolism
Choriocarcinoma: PA, pathology
Heparin: AA, analogs & derivatives
Heparin: AN, analysis
*Hydatidiform Mole: ME, metabolism
Hydatidiform Mole: PA, pathology
Hydatidiform Mole, Invasive: ME, metabolism
Hydatidiform Mole, Invasive: PA, pathology
Immunohistochemistry
Membrane Glycoproteins: AN, analysis
Neoplasm Proteins: AN, analysis
Pregnancy
Pregnancy Trimester, First
Pregnancy Trimester, Third
*Proteoglycans: AN, analysis
*Trophoblast: ME, metabolism
Trophoblast: PA, pathology
Uterine Neoplasms: ME, metabolism
Uterine Neoplasms: PA, pathology

L33 ANSWER 13 OF 33 CANCERLIT on STN
AN 1998380514 CANCERLIT
DN 98380514 PubMed ID: 9712917
TI Heparan sulfate proteoglycans as adhesive and anti-invasive molecules. Syndecans and glypican have distinct functions.
AU Liu W; Litwack E D; Stanley M J; Langford J K; Lander A D; Sanderson R D
CS Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA.
NC CA 55879 (NCI)
CA 68494 (NCI)
NS 26862 (NINDS)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Aug 28) 273 (35) 22825-32.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1998380514
EM 199809
ED Entered STN: 19981007
Last Updated on STN: 19981007
AB ARH-77 cells do not adhere to type I collagen and readily invade into collagen gels, but following expression of the transmembrane **heparan sulfate proteoglycan** syndecan-1, they bind collagen and fail to invade. We now show that cells transfected with syndecan-2 or syndecan-4 also bind collagen and are non-invasive. In contrast, cells transfected with the **glycosylphosphatidylinositol**-anchored proteoglycan **glypican-1** do not bind to collagen and remain invasive, even though glypican- and syndecan-expressing cells have similar surface levels of **heparan sulfate**, and their **proteoglycans** have similar affinities for collagen. Analysis of cells expressing syndecan-1-**glypican-1** chimeric proteoglycans reveals that inhibition of invasion requires the extracellular domain of syndecan but not its transmembrane or cytoplasmic domain. Surprisingly, cells bearing a chimera composed of the glypican extracellular domain fused to the syndecan transmembrane and cytoplasmic domains bind to collagen but remain invasive, implying that adhesion to collagen is not by itself sufficient to inhibit invasion. Apparently, the extracellular domain of syndecan-1, presumably by

interacting with cell-surface signal transducing molecules, directly regulates complex cell behaviors such as motility and invasiveness. These results also show for the first time that syndecans and glypicans can have distinct functions, even when expressed by the same cell type.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Cell Adhesion: PH, physiology
Cell Line
Chimeric Proteins: ME, metabolism
Collagen
Heparan Sulfate Proteoglycan: ME, metabolism
*Heparan Sulfate Proteoglycan: PH, physiology
Membrane Glycoproteins: ME, metabolism
*Membrane Glycoproteins: PH, physiology
*Neoplasm Invasiveness: PA, pathology
Proteoglycans: ME, metabolism
*Proteoglycans: PH, physiology
Rats
Structure-Activity Relationship

L33 ANSWER 14 OF 33 CANCERLIT on STN
AN 1999021665 CANCERLIT
DN 99021665 PubMed ID: 9802880
TI The cell-surface heparan sulfate proteoglycan **glypican-1** regulates growth factor action in pancreatic carcinoma cells and is overexpressed in human pancreatic cancer.
AU Kleeff J; Ishiwata T; Kumbasar A; Friess H; Buchler M W; Lander A D; Korc M
CS Departments of Medicine, Biological Chemistry, and Pharmacology, University of California, 92697, USA.
NC CA-40162 (NCI)
NS-26862 (NINDS)
SO JOURNAL OF CLINICAL INVESTIGATION, (1998 Nov 1) 102 (9) 1662-73.
Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Abridged Index Medicus Journals; Priority Journals
OS MEDLINE 1999021665
EM 199812
ED Entered STN: 19990127
Last Updated on STN: 19990127
AB **Heparan sulfate proteoglycans** (HSPGs) play diverse roles in cell recognition, growth, and adhesion. In vitro studies suggest that cell-surface HSPGs act as coreceptors for heparin-binding mitogenic growth factors. Here we show that the **glycosylphosphatidylinositol**- (GPI-) anchored HSPG **glypican-1** is strongly expressed in human pancreatic cancer, both by the cancer cells and the adjacent fibroblasts, whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors that are commonly overexpressed in pancreatic cancer: fibroblast growth factor 2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). PI-PLC did not alter the response to the non-heparin-binding growth factors EGF and IGF-1. Stable expression of a form of **glypican-1** engineered to possess a transmembrane domain instead of a GPI anchor conferred resistance to the inhibitory effects of PI-PLC on growth factor responsiveness. Furthermore, transfection of a **glypican-**

1 antisense construct attenuated **glypican-1**
protein levels and the mitogenic response to FGF2 and HB-EGF. We propose that **glypican-1** plays an essential role in the
responses of pancreatic cancer cells to certain mitogenic stimuli, that it is relatively unique in relation to other HSPGs, and that its expression by pancreatic cancer cells may be of importance in the pathobiology of this disorder.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adolescence
Adult
Aged
Aged, 80 and over
Amino Acid Sequence
Cell Membrane
Epidermal Growth Factor: ME, metabolism
Fibroblast Growth Factor 2: ME, metabolism
Gene Expression
Glycosylphosphatidylinositols: ME, metabolism
*Growth Substances: ME, metabolism
*Heparan Sulfate Proteoglycan: BI, biosynthesis
Immunoenzyme Techniques
In Situ Hybridization
Insulin-Like Growth Factor I: ME, metabolism
Middle Age
Molecular Sequence Data
*Pancreatic Neoplasms: ME, metabolism
Pancreatic Neoplasms: PA, pathology
Tumor Cells, Cultured

L33 ANSWER 15 OF 33 CANCERLIT on STN
AN 1998031917 CANCERLIT
DN 98031917 PubMed ID: 9362504
TI Glypican and biglycan in the nuclei of neurons and glioma cells: presence of functional nuclear localization signals and dynamic changes in glypican during the cell cycle.
AU Liang Y; Haring M; Roughley P J; Margolis R K; Margolis R U
CS Department of Pharmacology, New York University Medical Center, New York 10016, USA.
NC MH-00129 (NIMH)
NS-09348 (NINDS)
NS-13876 (NINDS)
SO JOURNAL OF CELL BIOLOGY, (1997 Nov 17) 139 (4) 851-64.
Journal code: 0375356. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1998031917
EM 199712
ED Entered STN: 19980109
Last Updated on STN: 19980109
AB We have investigated the expression patterns and subcellular localization in nervous tissue of glypican, a major **glycosylphosphatidylinositol**
*** -anchored ***heparan sulfate proteoglycan**
that is predominantly synthesized by neurons, and of biglycan, a small, leucine-rich chondroitin sulfate proteoglycan. By laser scanning confocal microscopy of rat central nervous tissue and C6 glioma cells, we found that a significant portion of the glypican and biglycan immunoreactivity colocalized with nuclear staining by propidium iodide and was also seen in

isolated nuclei. In certain regions, staining was selective, insofar as glypican and biglycan immunoreactivity in the nucleus was seen predominantly in a subpopulation of large spinal cord neurons. The amino acid sequences of both proteoglycans contain potential nuclear localization signals, and these were demonstrated to be functional based on their ability to target beta-galactosidase fusion proteins to the nuclei of transfected 293 cells. Nuclear localization of glypican beta-galactosidase or Fc fusion proteins in transfected 293 cells and C6 glioma cells was greatly reduced or abolished after mutation of the basic amino acids or deletion of the sequence containing the nuclear localization signal, and no nuclear staining was seen in the case of **heparan sulfate** and chondroitin **sulfate** **proteoglycans** that do not possess a nuclear localization signal, such as syndecan-3 or decorin (which is closely related in structure to biglycan). Transfection of COS-1 cells with an epitope-tagged glypican cDNA demonstrated transport of the full-length proteoglycan to the nucleus, and there are also dynamic changes in the pattern of glypican immunoreactivity in the nucleus of C6 cells both during cell division and correlated with different phases of the cell cycle. Our data therefore suggest that in certain cells and central nervous system regions, glypican and biglycan may be involved in the regulation of cell division and survival by directly participating in nuclear processes.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
*Cell Cycle
Cell Line
*Cell Nucleus: ME, metabolism
Fluorescent Antibody Technique, Indirect
*Glioma: ME, metabolism
Glioma: UL, ultrastructure
*Heparan Sulfate Proteoglycan: ME, metabolism
Microscopy, Confocal
*Neurons: ME, metabolism
Neurons: UL, ultrastructure
*Nuclear Localization Signal
*Nuclear Proteins: ME, metabolism
*Proteoglycans: ME, metabolism
Rats
Recombinant Proteins: ME, metabolism
Transfection

L33 ANSWER 16 OF 33 CANCERLIT on STN
AN 97278861 CANCERLIT
DN 97278861 PubMed ID: 9133439
TI Cerebroglycan, a developmentally regulated cell-surface heparan sulfate proteoglycan, is expressed on developing axons and growth cones.
AU Ivins J K; Litwack E D; Kumbasar A; Stipp C S; Lander A D
CS Department of Cell and Developmental Biology, University of California at Irvine, 92697, USA.. jkivins@UCI.edu
NC NS26862 (NINDS)
SO DEVELOPMENTAL BIOLOGY, (1997 Apr 15) 184 (2) 320-32.
Journal code: 0372762. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 97278861
EM 199706
ED Entered STN: 19970711
Last Updated on STN: 19970711
AB Cerebroglycan is a **glycosylphosphatidylinositol**-linked integral

membrane **heparan sulfate proteoglycan** found exclusively in the developing nervous system. In the rodent, cerebroglycan mRNA first appears in regions containing newly generated neurons and typically disappears 1 to several days later (Stipp et al., 1994, J. Cell Biol. 124:149-160). To gain insight into the roles that cerebroglycan plays in the developing nervous system, monospecific antibodies were prepared and used to localize cerebroglycan protein. In the rat, cerebroglycan was prominantly expressed on axon tracts throughout the developing brain and spinal cord, where it was found at times when axons are actively growing, but generally not after axons have reached their targets. Cerebroglycan was also found on neuronal growth cones both in vivo and in vitro. Interestingly, cerebroglycan immunoreactivity was rarely seen in or around neuronal cell bodies. Indeed, by examining the hippocampus at a late stage in development-when most neurons no longer express cerebroglycan but newly generated granule neurons do-evidence was obtained that cerebroglycan is strongly polarized to the axonal, and excluded from the somatodendritic, compartment of neurons. The timing and pattern of cerebroglycan expression are consistent with a role for this cell-surface **heparan sulfate proteoglycan** in regulating the growth or guidance of axons.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Axons: CH, chemistry
*Axons: PH, physiology
Blotting, Western
Brain: EM, embryology
Brain: ME, metabolism
Cells, Cultured
Chondroitin Lyases: ME, metabolism
Dentate Gyrus: EM, embryology
Dentate Gyrus: ME, metabolism
*Gene Expression Regulation, Developmental
Heparitin Sulfate: ME, metabolism
Immunochemistry
In Situ Hybridization
Membrane Proteins: AN, analysis
Membrane Proteins: CH, chemistry
Membrane Proteins: GE, genetics
Membrane Proteins: ME, metabolism
*Membrane Proteins: PH, physiology
Neurons: CH, chemistry
*Neurons: CY, cytology
PC12 Cells
Polysaccharide-Lyases: ME, metabolism
Proteoglycans: AN, analysis
Proteoglycans: GE, genetics
Proteoglycans: ME, metabolism
*Proteoglycans: PH, physiology
RNA, Messenger: ME, metabolism
Rats
Rats, Sprague-Dawley
Spinal Cord: EM, embryology
Spinal Cord: ME, metabolism

L33 ANSWER 17 OF 33 CANCERLIT on STN
AN 95213323 CANCERLIT
DN 95213323 PubMed ID: 7699018
TI Immunocytochemical and in situ hybridization studies of the heparan sulfate proteoglycan, glypican, in nervous tissue.
AU Karthikeyan L; Flad M; Engel M; Meyer-Puttlitz B; Margolis R U; Margolis R K

CS Department of Pharmacology, New York University Medical Center, NY 10016.
NC MH-00129 (NIMH)
NS-09348 (NINDS)
NS-13876 (NINDS)
SO JOURNAL OF CELL SCIENCE, (1994 Nov) 107 (Pt 11) 3213-22.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 95213323
EM 199505
ED Entered STN: 19950608
Last Updated on STN: 19970509
AB Using immunocytochemistry and in situ hybridization histochemistry, we have investigated in embryonic and postnatal rat nervous tissue the localization and cellular sites of synthesis of glypican, a **glycosylphosphatidylinositol**-anchored **heparan sulfate proteoglycan.** Glypican immunoreactivity is present in the marginal layer (prospective white matter) and in the dorsal root entry zone of E13-16 spinal cord, as well as in the optic nerve and retina at this stage, but does not appear at significant levels in brain until approximately E19. The proteoglycan shows a wide distribution in grey matter and axonal projections of postnatal brain, including the hippocampal formation, the parallel fibers of cerebellar granule cells, and in the medulla and brainstem. Northern analysis demonstrated high levels of glypican mRNA in brain and skeletal muscle, and in rat PC12 pheochromocytoma cells. In situ hybridization histochemistry showed that glypican mRNA was especially prominent in cerebellar granule cells, large motor neurons in the brainstem, and CA3 pyramidal cells of the hippocampus. Our immunocytochemical and in situ hybridization results indicate that glypican is predominantly a neuronal membrane proteoglycan in the late embryonic and postnatal rat central nervous system.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Amino Acid Sequence
Fluorescent Antibody Technique
Gestational Age
Heparan Sulfate Proteoglycan
Heparitin Sulfate: GE, genetics
Heparitin Sulfate: IM, immunology
*Heparitin Sulfate: ME, metabolism
Immunohistochemistry
In Situ Hybridization
Molecular Sequence Data
Nervous System: EM, embryology
*Nervous System: ME, metabolism
PC12 Cells
Proteoglycans: GE, genetics
Proteoglycans: IM, immunology
*Proteoglycans: ME, metabolism
RNA, Messenger: GE, genetics
RNA, Messenger: ME, metabolism
Rats
Tissue Distribution

L33 ANSWER 18 OF 33 CANCERLIT on STN
AN 94208544 CANCERLIT
DN 94208544 PubMed ID: 7512501
TI Release of GPI-anchored membrane proteins by a cell-associated GPI-specific phospholipase D.

AU Metz C N; Brunner G; Choi-Muira N H; Nguyen H; Gabrilove J; Caras I W; Altszuler N; Rifkin D B; Wilson E L; Davitz M A
CS Department of Pathology, New York University Medical Center, NY 10016.
NC CA 34282 (NCI)
CA 49419 (NCI)
SO EMBO JOURNAL, (1994 Apr 1) 13 (7) 1741-51.
Journal code: 8208664. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 94208544
EM 199405
ED Entered STN: 19990618
Last Updated on STN: 19990618
AB Although many **glycosylphosphatidylinositol** (GPI)-anchored proteins have been observed as soluble forms, the mechanisms by which they are released from the cell surface have not been demonstrated. We show here that a cell-associated GPI-specific phospholipase D (GPI-PLD) releases the GPI-anchored, complement regulatory protein decay-accelerating factor (DAF) from HeLa cells, as well as the basic fibroblast growth factor-binding **heparan sulfate proteoglycan** from bone marrow stromal cells. DAF found in the HeLa cell culture supernatants contained both [3H]ethanolamine and [3H]inositol, but not [3H]palmitic acid, whereas the soluble **heparan sulfate proteoglycan** present in bone marrow stromal cell culture supernatants contained [3H]ethanolamine. 125I-labeled GPI-DAF incorporated into the plasma membranes of these two cell types was released in a soluble form lacking the fatty acid GPI-anchor component. GPI-PLD activity was detected in lysates of both HeLa and bone marrow stromal cells. Treatment of HeLa cells with 1,10-phenanthroline, an inhibitor of GPI-PLD, reduced the release of [3H]ethanolamine-DAF by 70%. The hydrolysis of these GPI-anchored molecules is likely to be mediated by an endogenous GPI-PLD because [3H]ethanolamine DAF is constitutively released from HeLa cells maintained in serum-free medium. Furthermore, using PCR, a GPI-PLD mRNA has been identified in cDNA libraries prepared from both cell types. These studies are the first demonstration of the physiologically relevant release of GPI-anchored proteins from cells by a GPI-PLD.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Antigens, CD: ME, metabolism
Antigens, CD55
Bone Marrow: EN, enzymology
Bone Marrow Cells
DNA, Complementary: GE, genetics
Ethanolamine
Ethanolamines: ME, metabolism
Gene Library
*Glycosylphosphatidylinositols: ME, metabolism
Hela Cells: EN, enzymology
Heparan Sulfate Proteoglycan
*Heparitin Sulfate: ME, metabolism
Inositol: ME, metabolism
*Membrane Glycoproteins: ME, metabolism
Phenanthrolines: PD, pharmacology
Phospholipase D: AI, antagonists & inhibitors
Phospholipase D: GE, genetics
*Phospholipase D: ME, metabolism
*Proteoglycans: ME, metabolism
RNA, Messenger: GE, genetics

L33 ANSWER 19 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2005:114934 BIOSIS
DN PREV200500113076
TI Constitutive release of alpha4 type V collagen N-terminal domain by Schwann cells and binding to cell surface and extracellular matrix heparan sulfate proteoglycans.
AU Rothblum, Katrina; Stahl, Richard C.; Carey, David J. [Reprint Author]
CS Weis Ctr Res, Geisinger Clin, 100 N Acad Ave, Danville, PA, 17822, USA
djcarey@geisinger.edu
SO Journal of Biological Chemistry, (December 3 2004) Vol. 279, No. 49, pp. 51282-51288. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 23 Mar 2005
Last Updated on STN: 23 Mar 2005
AB During peripheral nerve development, Schwann cells synthesize collagen type V molecules that contain alpha4(V) chains. This collagen subunit possesses an N-terminal domain (NTD) that contains a unique high affinity heparin binding site. The alpha4(V)-NTD is adhesive for Schwann cells and sensory neurons and is an excellent substrate for Schwann cell and axonal migration. Here we show that the alpha4(V)-NTD is released constitutively by Schwann cells both in culture and in vivo. In cultures of neonatal rat Schwann cells, alpha4(V)-NTD release is increased significantly by ascorbate treatment, which facilitates collagen post-translational modification and collagen trimer assembly. In peripheral nerve tissue, the alpha4(V)-NTD is localized to the region of the outer Schwann cell membrane and associated extracellular matrix. The released alpha4(V)-NTD binds to the cell surface and extracellular matrix heparan sulfate proteoglycans of Schwann cells. Pull-down assays and immunofluorescent staining showed that the major alpha4(V)-NTD-**binding proteins** are **glypican-1** and perlecan.
alpha4(V)-NTD binding occurs via a mechanism that requires the high affinity heparin binding site and that is blocked by soluble heparin, demonstrating that binding to proteoglycans is mediated by their heparan sulfate chains.
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
Schwann cell: nervous system; cell surface; peripheral nerve: nervous system; sensory neuron: nervous system
IT Chemicals & Biochemicals
alpha-4; ascorbate; collagen: trimer assembly; collagen type V: N-terminal domain; **glypican-1**; heparan sulfate; heparan sulfate proteoglycans: extracellular matrix; perlecan

L33 ANSWER 20 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2004:451251 BIOSIS
DN PREV200400454030
TI Expression of CD44v3 protein in human endothelial cells in vitro and in **tumoral** microvessels in vivo.
AU Forster-Horvath, C.; Meszaros, L.; Raso, E.; Dome, B.; Ladanyi, A.; Morini, M.; Albini, A.; Timar, J. [Reprint Author]
CS Dept Tumor Progress, Natl Inst Oncol, Rath Gyorgy 7-9, H-1122, Budapest, Hungary
jtimar@oncol.hu

SO Microvascular Research, (September 2004) Vol. 68, No. 2, pp. 110-118. print.
CODEN: MIVRA6. ISSN: 0026-2862.
DT Article
LA English
ED Entered STN: 24 Nov 2004
Last Updated on STN: 24 Nov 2004
AB The most universal angiogenic cytokines (VEGF, bFGF, HGF) are all heparin-**binding proteins**, the function of which is dependent on cell surface heparan sulfate proteoglycans (HSPG). Several proteoglycans have been demonstrated in endothelial cells, but only **glypican-1** from the cell surface HSPG subfamily was documented at protein level. Here, we show that CD44v3 is expressed in human immortalized endothelial cells (anchorage-dependent human umbilical vein endothelial cells (HUVEC) and anchorage-independent Kaposi sarcoma (KS-Imm)) at mRNA and protein level, but is absent from the primary culture of human brain microvascular endothelial cells. We have shown that CD44v3 has a large cytoplasmic pool in endothelial cells, but a limited surface expression, mainly at filopodia, colocalized with MMP-2. Angiogenic factors like VEGF or bFGF did not affect surface detection of CD44v3 suggesting a constitutive expression. The putative functional role for endothelial cell surface CD44v3 was identified in chemotaxis assay when anti-CD44v3 antibody pretreatment proved to be inhibitory for HUVEC. Furthermore, we provided evidence for the CD44v3 protein expression in human endothelial cells in vivo in peritumoral microvessels of both human melanoma and glottic **cancers**, suggesting a role for this part-time heparan sulfate proteoglycan in **tumor** induced angiogenesis.
IT Major Concepts
Cardiovascular System (Transport and Circulation); **Tumor** Biology
IT Parts, Structures, & Systems of Organisms
endothelial cell: circulatory system; microvessel: circulatory system
IT Diseases
Kaposi sarcoma: **neoplastic** disease
Sarcoma, Kaposi (MeSH)
IT Chemicals & Biochemicals
CD44v3 protein; MMP-2 [matrix metalloproteinase-2]; basic fibroblast growth factor: cytokine; heparan sulfate proteoglycan; hepatocyte growth factor: cytokine; mRNA [messenger RNA]; vascular endothelial growth factor: cytokine

L33 ANSWER 21 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:537579 BIOSIS
DN PREV200300524443
TI Interaction of low molecular weight group IIA phospholipase A2 with apoptotic human T cells: Role of heparan sulfate proteoglycans.
AU Boilard, Eric; Bourgoin, Sylvain G.; Bernatchez, Chantale; Poubelle, Patrice E.; Surette, Marc E. [Reprint Author]
CS Pilot Therapeutics Inc., 2000 Daniel Island Dr., Suite 440, Charleston, SC, 29492, USA
MarcS@pilott.com
SO FASEB Journal, (June 2003) Vol. 17, No. 9, pp. 1068-1080. http://www.fasebj.org/. online.
ISSN: 0892-6638 (ISSN print).
DT Article
LA English
ED Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

AB Human group IIA phospholipase A2 (hIIA PLA2) is a 14 kDa secreted enzyme associated with inflammatory diseases. A newly discovered property of hIIA PLA2 is the binding affinity for the heparan sulfate proteoglycan (HSPG) **glypican-1.** In this study, the binding of hIIA PLA2 to apoptotic human T cells was investigated. Little or no exogenous hIIA PLA2 bound to CD3-activated T cells but significant binding was measured on activated T cells induced to undergo apoptosis by anti-CD95. Binding to early apoptotic T cells was greater than to late apoptotic cells. The addition of heparin and the hydrolysis of HSPG by heparinase III only partially inhibited hIIA PLA2 binding to apoptotic cells, suggesting an interaction with both HSPG and other **binding protein**(s). Two low molecular weight HSPG were coimmunoprecipitated with hIIA PLA2 from apoptotic T cells, but not from living cells. Treatment of CD95-stimulated T cells with hIIA PLA2 resulted in the release of arachidonic acid but not oleic acid from cells and this release was blocked by heparin and heparinase III. Altogether, these results suggest a role for hIIA PLA2 in the release of arachidonic acid from apoptotic cells through interactions with HSPG and its potential implication in the progression of inflammatory diseases.

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis)

IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system, apoptotic

IT Chemicals & Biochemicals
anti-CD95; arachidonic acid: release; heparan sulfate proteoglycans; heparin; heparinase III [EC 4.2.2.8]; oleic acid: release; phospholipase A-2 [EC 3.1.1.4]: low-molecular weight group II

L33 ANSWER 22 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2003:331425 BIOSIS

DN PREV200300331425

TI Comparison of expression patterns between CREB family transcription factor OASIS and proteoglycan core protein genes during murine tooth development.

AU Hikake, Tsuyoshi; Mori, Tetsuji; Iseki, Ken; Hagino, Seita; Zhang, Yuxiang; Takagi, Hiromi; Yokoya, Sachihiko; Wanaka, Akio [Reprint Author]

CS Department of Anatomy, Nara Medical University, 634-8521, Nara, Japan akiow@naramed-u.ac.jp

SO Anatomy and Embryology, (April 2003) Vol. 206, No. 5, pp. 373-380. print. ISSN: 0340-2061 (ISSN print).

DT Article

LA English

OS DDBJ-AA386748; EMBL-AA386748; GenBank-AA386748; DDBJ-AA562747; EMBL-AA562747; GenBank-AA562747; DDBJ-AA671369; EMBL-AA671369; GenBank-AA671369; DDBJ-AA691493; EMBL-AA691493; GenBank-AA691493; DDBJ-AA855868; EMBL-AA855868; GenBank-AA855868; DDBJ-AI019805; EMBL-AI019805; GenBank-AI019805; DDBJ-AI266824; EMBL-AI266824; GenBank-AI266824; DDBJ-AI323043; EMBL-AI323043; GenBank-AI323043; DDBJ-AI639805; EMBL-AI639805; GenBank-AI639805; DDBJ-AI893308; EMBL-AI893308; GenBank-AI893308; DDBJ-AI894071; EMBL-AI894071; GenBank-AI894071; DDBJ-AU080821; EMBL-AU080821; GenBank-AU080821; DDBJ-AW321523; EMBL-AW321523; GenBank-AW321523; DDBJ-BF385683; EMBL-BF385683; GenBank-BF385683; DDBJ-BF682284; EMBL-BF682284; GenBank-BF682284; DDBJ-T14904; EMBL-T14904; GenBank-T14904; DDBJ-W18139; EMBL-W18139; GenBank-W18139; DDBJ-W74978; EMBL-W74978; GenBank-W74978; DDBJ-W79980; EMBL-W79980; GenBank-W79980

ED Entered STN: 16 Jul 2003
Last Updated on STN: 22 Aug 2003

AB The transcription factor OASIS gene, which encodes for a CREB/ATF family

member, is specifically expressed in the salivary gland, the cartilage and the tooth germs of the mouse embryo. In the present study, the expression patterns were compared between OASIS mRNA and major vertebrate proteoglycans, which might be the downstream genes of OASIS in the tooth germs of mouse first mandibular molars, through in situ hybridization histochemistry. OASIS mRNA expression was observed in the inner enamel epithelium during the cap and bell stages (E14.5-E18.5) in the preodontoblasts during differentiation stage (E18.5-P0) and in the differentiating odontoblasts during the early secretory stage (P2.5-P4.5). Proteoglycans (versican, decorin, biglycan, **glypican**, syndecan-**1**, and syndecan-3) were expressed in the tooth germs in various patterns. Decorin, biglycan, syndecan-1 and syndecan-3 showed gene expressions overlapping with OASIS. Especially the expression pattern of decorin and syndecan-3 coincided temporally and spatially exactly with that of OASIS. These results suggest that the OASIS gene might be related to proteoglycan expression and may play an important role in the differentiation of the odontoblast and cells in inner enamel epithelium.

IT Major Concepts
Dental and Oral System (Ingestion and Assimilation); Development; Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
inner enamel epithelium: dental and oral system; mandibular molar: dental and oral system; odontoblasts: dental and oral system, differentiation; preodontoblasts: dental and oral system; tooth: dental and oral system, development; tooth germ: dental and oral system

IT Chemicals & Biochemicals
OASIS: CREB/ATF family transcription factor, cyclic AMP-response element **binding protein**/activating transcription factor family transcription factor; OASIS mRNA [OASIS messenger RNA]; biglycan: proteoglycan; decorin: proteoglycan; glypican: proteoglycan; syndecan-1: proteoglycan; syndecan-3: proteoglycan; versican: proteoglycan

L33 ANSWER 23 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:470709 BIOSIS
DN PREV200300470709
TI Expression pattern of **glypican**-1 mRNA after brain injury in mice.
AU Hagino, Seita [Reprint Author]; Iseki, Ken; Mori, Tetsuji; Zhang, Yuxiang; Sakai, Nobuko; Yokoya, Sachihiko; Hikake, Tsuyoshi; Kikuchi, Shinichi; Wanaka, Akio
CS Department of Orthopedic Surgery, School of Medicine, Fukushima Medical University, Fukushima, 960-1295, Japan
shagino@fmu.ac.jp
SO Neuroscience Letters, (September 25 2003) Vol. 349, No. 1, pp. 29-32. print.
ISSN: 0304-3940 (ISSN print).
DT Article
LA English
ED Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003
AB **Glypican-1**, a heparan sulfate proteoglycan, is expressed in various tissues including developing and postnatal central nervous system. It serves as a receptor for heparin-**binding molecules** such as fibroblast growth factors (FGFs). We investigated whether **glypican-1** was expressed after brain injury in adult mice. In situ hybridization study showed that **glypican-1** mRNA was expressed in the region surrounding necrotic tissue, and that the signal intensity peaked 7 days after the

cryo-injury. In addition, both FGF-2 and amyloid precursor protein (APP) were concurrently upregulated and colocalized with **glypican-1** mRNA. Since FGF-2 and APP can bind to **glypican-1** in vitro, the present study suggested that their autocrine/paracrine interactions with **glypican-1** may be involved in neuronal regeneration and/or neurite-outgrowth inhibition after brain injury.

IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination)

IT Parts, Structures, & Systems of Organisms
neurite: nervous system, outgrowth

IT Diseases
brain injury: injury, nervous system disease
Brain Injuries (MeSH)

IT Chemicals & Biochemicals
amyloid precursor protein [APP]; fibroblast growth factor [FGF]; fibroblast growth factor-2 [FGF-2]; **glypican-1**; **glypican-1** mRNA [**glypican-1** messenger RNA]: expression

L33 ANSWER 24 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2001:434957 BIOSIS

DN PREV200100434957

TI The surface antigen SAG3 mediates the attachment of Toxoplasma gondii to cell-surface proteoglycans.

AU Jacquet, Alain [Reprint author]; Coulon, Ludivine; De Neve, Joel; Daminet, Veronique; Haumont, Michele; Garcia, Lida; Bollen, Alex; Jurado, Margarita; Biemans, Ralph

CS Department of Applied Genetics, Institut de Biologie et de Medicine Moleculaires, Universite Libre de Bruxelles, Rue des Professeurs Jeener et Brachet 12, B-6041, Gosselies, Belgium
ajacquet@sga.ulb.ac.be

SO Molecular and Biochemical Parasitology, (August, 2001) Vol. 116, No. 1, pp. 35-44. print.
CODEN: MBIPDP. ISSN: 0166-6851.

DT Article

LA English

ED Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002

AB The attachment of Toxoplasma gondii to target cells is mediated by recognition of cellular **heparan sulfate proteoglycans** (HSPGs). The present study was performed to determine whether SAG1 and SAG3, two of the parasite surface antigens anchored to the membrane via **glycosylphosphatidylinositol** groups (GPIs), are involved in the tachyzoite binding to proteoglycans. The use of recombinant soluble forms of these proteins allowed us to demonstrate that SAG3, but not SAG1, interacts specifically with cellular HSPGs. Indeed, soluble recombinant SAG3 protein (recSAG3) was found to bind to immobilized heparin, whereas recSAG1 did not interact with this glycoaminoglycan. The specific adherence of recSAG3 to CHO cells was inhibited by soluble glycoconjugates, of which heparin, fucoidan and dextran sulfate were the most effective. Moreover, binding of recSAG3 to two HSPGs-deficient cell mutants was reduced by up to 80%. Proteoglycan sulfation was critical for SAG3 adherence to HSPGs as incubation of cells in the presence of sodium chlorate drastically reduced the recSAG3 binding. Finally, preincubation of CHO cells with recSAG3 blocked the adsorption of radiolabelled Toxoplasma tachyzoites. Taken together, these results indicate that SAG3 is a first glycoaminoglycan-**binding**

protein associated with Toxoplasma, and SAG3-HSPGs interactions are involved in the parasite attachment to target cells.

IT Major Concepts
Cell Biology; Immune System (Chemical Coordination and Homeostasis); Parasitology

IT Chemicals & Biochemicals
SAG1; cell surface proteoglycans; glycosylphosphatidylinositol groups; heparin; surface antigen SAG3: recombinant, soluble

L33 ANSWER 25 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1999:349456 BIOSIS

DN PREV199900349456

TI Mammalian homologues of the Drosophila Slit protein are ligands of the heparan sulfate proteoglycan **glypican-1** in brain.

AU Liang, Yu; Annan, Roland S.; Carr, Steven A.; Popp, Susanna; Mevissen, Markus; Margolis, Renee K.; Margolis, Richard U. [Reprint author]

CS Dept. of Pharmacology, New York University School of Medicine, 550 First Ave., New York, NY, 10016, USA

SO Journal of Biological Chemistry, (June 18, 1999) Vol. 274, No. 25, pp. 17885-17892. print.
CODEN: JBCHA3. ISSN: 0021-9258.

DT Article

LA English

OS Genbank-AF141386

ED Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

AB Using an affinity matrix in which a recombinant glypican-Fc fusion protein expressed in 293 cells was coupled to protein A-Sepharose, we have isolated from rat brain at least two proteins that were detected by SDS-polyacrylamide gel electrophoresis as a single 200-kDa silver-stained band, from which 16 partial peptide sequences were obtained by nano-electrospray tandem mass spectrometry. Mouse expressed sequence tags containing two of these peptides were employed for oligonucleotide design and synthesis of probes by polymerase chain reaction and enabled us to isolate from a rat brain cDNA library a 4.1-kilobase clone that encoded two of our peptide sequences and represented the N-terminal portion of a protein containing a signal peptide and three leucine-rich repeats. Comparisons with recently published sequences also showed that our peptides were derived from proteins that are members of the Slit/MEGF protein family, which share a number of structural features such as N-terminal leucine-rich repeats and C-terminal epidermal growth factor-like motifs, and in Drosophila Slit is necessary for the development of midline glia and commissural axon pathways. All of the five known rat and human Slit proteins contain 1523-1534 amino acids, and our peptide sequences correspond best to those present in human Slit-1 and Slit-2. Binding of these ligands to the glypican-Fc fusion protein requires the presence of the heparan sulfate chains, but the interaction appears to be relatively specific for **glypican-1** insofar as no other identified heparin-**binding proteins** were isolated using our affinity matrix. Northern analysis demonstrated the presence of two mRNA species of 8.6 and 7.5 kilobase pairs using probes based on both N- and C-terminal sequences, and in situ hybridization histochemistry showed that these **glypican-1** ligands are synthesized by neurons, such as hippocampal pyramidal cells and cerebellar granule cells, where we have previously also demonstrated **glypican-1** mRNA and immunoreactivity. Our results therefore indicate that Slit family proteins are functional ligands of **glypican-1** in nervous tissue and suggest that their interactions may be critical for

certain stages of central nervous system histogenesis.
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: nervous system; nervous tissue: nervous system, axonal pathfinding, histogenesis
IT Chemicals & Biochemicals
glypican-1: heparan sulfate proteoglycan; mammalian
Slit proteins: Drosophila homolog, **glypican-1**
ligand; Drosophila Slit proteins: **glypican-1** ligand

L33 ANSWER 26 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1999:141196 BIOSIS
DN PREV199900141196
TI Interactions of neural glycosaminoglycans and proteoglycans with protein ligands: Assessment of selectivity, heterogeneity and the participation of core proteins in binding.
AU Herndon, Mary E. [Reprint author]; Stipp, Christopher S.; Lander, Arthur D.
CS Dep. Exp. Pathol., Beth Israel Deaconess Med. Cent., RN-287, Boston, MA 02215, USA
SO Glycobiology, (Feb., 1999) Vol. 9, No. 2, pp. 143-155. print.
ISSN: 0959-6658.
DT Article
LA English
ED Entered STN: 31 Mar 1999
Last Updated on STN: 31 Mar 1999
AB The method of affinity coelectrophoresis was used to study the binding of nine representative glycosaminoglycan (GAG)-**binding proteins**, all thought to play roles in nervous system development, to GAGs and proteoglycans isolated from developing rat brain. Binding to heparin and non-neural heparan and chondroitin sulfates was also measured. All nine proteins-laminin-1, fibronectin, thrombospondin-1, NCAM, L1, protease nexin-1, urokinase plasminogen activator, thrombin, and fibroblast growth factor-2-bound brain heparan sulfate less strongly than heparin, but the degree of difference in affinity varied considerably. Protease nexin-1 bound brain heparan sulfate only 1.8-fold less tightly than heparin (Kd values of 35 vs. 20 nM, respectively), whereas NCAM and L1 bound heparin well (Kd apprx140 nM) but failed to bind detectably to brain heparan sulfate (Kd > 3 muM). Four proteins bound brain chondroitin sulfate, with affinities equal to or a few fold stronger than the same proteins displayed toward cartilage chondroitin sulfate. Overall, the highest affinities were observed with intact heparan sulfate proteoglycans: laminin-1's affinities for the proteoglycans cerebroglycan (**glypican**-2), **glypican-1** and syndecan-3 were 300- to 1800-fold stronger than its affinity for brain heparan sulfate. In contrast, the affinities of fibroblast growth factor-2 for cerebroglycan and for brain heparan sulfate were similar. Interestingly, partial proteolysis of cerebroglycan resulted in a >400-fold loss of laminin affinity. These data support the views that (1) GAG-**binding proteins** can be differentially sensitive to variations in GAG structure, and (2) core proteins can have dramatic, ligand-specific influences on protein-proteoglycan interactions.
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: nervous system, developing

IT Chemicals & Biochemicals
cerebroglycan; chondroitin sulfate; fibroblast growth factor-2; fibronectin; glycosaminoglycan; glycosaminoglycan-**binding proteins**; **glypican-1**; glypican-2; heparin; laminin-1; non-neural heparan; protease nexin-1; proteoglycans; syndecan-3; thrombin; thrombospondin-1; urokinase plasminogen activator; L1; NCAM

L33 ANSWER 27 OF 33 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1996:434458 BIOSIS
DN PREV199699148064
TI Cell-surface expression of an amino-terminal fragment of apolipoprotein B increases lipoprotein lipase binding to cells.
AU Pang, Ling; Sivaram, Pillarisetti; Goldberg, Ira J. [Reprint author]
CS Dep. Med., Columbia University, College Physicians Surgeons, 630 West 168th St., New York, NY 10032, USA
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 32, pp. 19518-19523. CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 26 Sep 1996
Last Updated on STN: 26 Sep 1996
AB Previous studies (Sivaram, P., Choi, S. Y., Curtiss, L. K., and Goldberg, I. J. (1994) J. Biol. Chemical 269, 9409-9412) from this laboratory showed that the NH-2-terminal region of apoB (NTAB) has binding domains for lipoprotein lipase (LPL). LPL binding to endothelial cells, we hypothesize, involves interaction both with **heparan sulfate proteoglycans** and with a protein that has homology to NTAB. To test whether cell-surface NTAB would increase the amount and affinity of LPL binding to cells, we produced stable Chinese hamster ovary cell lines that have NTAB anchored to the cell surface. A cDNA encoding the amino-terminal 17% of apoB (apoB17) was fused to a cDNA coding for the last 37 amino acids of decay-accelerating factor (DAF), which contains the signal for **glycosylphosphatidylinositol** anchor attachment. The fused construct was sequence-verified and cloned into expression vector pCMV5. The pCMV5-apoB17-DAF plasmid was cotransfected with a neomycin resistance gene into wild-type (WT) cells and mutant **heparan sulfate proteoglycan** -deficient Chinese hamster ovary cells (745 cells), and stable cell lines were established. Expression of apoB17 on the cell surface was confirmed by the release of apoB17 by phosphatidylinositol-specific phospholipase C. LPL binding to WT and apoB17-DAF-transfected cells was determined. Using 0.8-6 mu-g of LPL, 1.3-2.2-fold more LPL associated with apoB17-DAF WT cells compared with WT cells; apoB17-DAF also increased LPL binding to 745 cells. After heparinase treatment, LPL binding to apoB17-DAF cells was still greater than to treated WT cells. This increased binding to apoB17-DAF cells was almost abolished by treatment of cells with phosphatidylinositol-specific phospholipase C or anti-apoB monoclonal antibody. LPL dissociated from WT cells with k-1 = 2.55 times 10-2 min-1, whereas LPL dissociated more slowly from apoB17-DAF-containing cells with k-1 = 1.08 times 10-2 min-1. Furthermore, almost 95% of the LPL on WT cells was dissociated by 1 M NaCl, while only 65% of the LPL dissociated from apoB17-DA.F cells at the same high salt concentration. Similarly, in high salt, more LPL remained associated with apoB17DAF cells than with nontransfected 745 cells. These data show that NTAB on cell surfaces can function as a LPL-**binding protein.** Moreover, they demonstrate that LPL association with cells can be increased by simultaneously binding to both proteoglycan and non-proteoglycan binding sites.

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology); Metabolism
IT Chemicals & Biochemicals
LIPOPROTEIN LIPASE

L33 ANSWER 28 OF 33 MEDLINE on STN
AN 2003139624 MEDLINE
DN PubMed ID: 12655597
TI Slit and **glypican-1** mRNAs are coexpressed in the reactive astrocytes of the injured adult brain.
AU Hagino Seita; Iseki Ken; Mori Tetsuji; Zhang Yuxiang; Hikake Tsuyoshi; Yokoya Sachihiko; Takeuchi Mayumi; Hasimoto Hiromi; Kikuchi Shinichi; Wanaka Akio
CS Department of Orthopedic Surgery, Fukushima Medical University School of Medicine, Fukushima, Japan.. shagino@fmu.ac.jp
SO Glia, (2003 Apr 15) 42 (2) 130-8.
Journal code: 8806785. ISSN: 0894-1491.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20030326
Last Updated on STN: 20030611
Entered Medline: 20030610
AB The slit family serves as a repellent for growing axons toward correct targets during neural development. A recent report describes slit mRNAs expressed in various brain regions in adult rats. However, their functions in the adult nervous system remain unknown. In the present study, we investigated whether slit mRNAs were expressed in the cryo-injured brain, using in situ hybridization. All slit family members were expressed at the lesion. Slit2 mRNA was the most intensely expressed in the cells surrounding the necrotic tissue. A double-labeling study showed that slit2 mRNA was expressed in the glial fibrillary acidic protein (GFAP)-positive reactive astrocytes. In addition, **glypican-1**, a heparan sulfate proteoglycan that serves as a high-affinity receptor for Slit protein, was coexpressed with slit2 mRNA in the reactive astrocytes. These findings suggested that slit2 might prevent regenerating axons from entering into the lesion in concert with **glypican-1.**

CT Check Tags: Male
Animals
Antigens, CD: ME, metabolism
Astrocytes: CY, cytology
*Astrocytes: ME, metabolism
Biological Markers
Brain Injuries: GE, genetics
*Brain Injuries: ME, metabolism
Brain Injuries: PP, physiopathology
Calcium-Binding Proteins: ME, metabolism
Gene Expression Regulation: PH, physiology
Glial Fibrillary Acidic Protein: ME, metabolism
Gliosis: GE, genetics
*Gliosis: ME, metabolism
Gliosis: PP, physiopathology
*Growth Cones: ME, metabolism
*Heparan Sulfate Proteoglycan: GE, genetics

Immunohistochemistry
Membrane Proteins: GE, genetics
Membrane Proteins: ME, metabolism
Mice
Mice, Inbred ICR
Microglia: CY, cytology
Microglia: ME, metabolism
*Nerve Regeneration: GE, genetics
*Nerve Tissue Proteins: GE, genetics
Oligodendroglia: CY, cytology
Oligodendroglia: ME, metabolism
RNA, Messenger: ME, metabolism
Research Support, Non-U.S. Gov't

L33 ANSWER 29 OF 33 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004424639 EMBASE
TI Mammalian and Drosophila cells adhere to the laminin α4 LG4 domain through syndecans, but not glypicans.
AU Yamashita H.; Goto A.; Kadowaki T.; Kitagawa Y.
CS Y. Kitagawa, Grad. Courses for Reg. Biol. Signals, Grad. Sch. of Bioagricultural Sci., Nagoya University, Nagoya 464-8601, Japan. yasuok@agr.nagoya-u.ac.jp
SO Biochemical Journal, (15 Sep 2004) Vol. 382, No. 3, pp. 933-943.
Refs: 47
ISSN: 0264-6021 CODEN: BIJOAK
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20041028
Last Updated on STN: 20041028
AB We have previously shown that the LG4 (laminin G-like) domain of the laminin α4 chain is responsible for the significantly higher affinity of the α4 chain to heparin than found for other α chains [Yamaguchi, Yamashita, Mori, Okazaki, Nomizu, Beck and Kitagawa (2000) J. Biol. Chemical 275, 29458-29465]; four basic residues were identified to be essential for this activity [Yamashita, Beck and Kitagawa (2004) J. Mol. Biol. 335, 1145-1149]. By creating GST (glutathione S-transferase)-fused LG1, LG2, LG4 and LG5 proteins, we found that only LG4 is active for the adhesion of human HT1080 cells, human umbilical vein endothelial cells and Drosophila haemocytes Kc167 with a half-saturating concentration of 20 μg/ml. Adhesion was counteracted by treatment of the cells with heparin, heparan sulphate and heparitinase I. Upon mutating the four basic residues essential for heparin binding within LG4, the adhesion activity was abolished. Pull-down experiments using glutathione beads/GST-fusion proteins indicate a direct interaction of LG4 with syndecan-4, which might be the major receptor for cell adhesion. Neither the release of **glypican-1** by treating human cells with phosphatidylinositol-specific phospholipase C nor targeted knockdown of dally or dally-like protein impaired the cell-adhesion activity. As the LG4-LG5 domain of the α4 chain is cleaved in vivo from the main body of laminin-8 (α4β1γ1), we suggest that the heparan sulphate proteoglycan-binding activity of LG4 is significant in modulating the signalling of Wnt, Decapentaplegic and fibroblast growth factors.
CT Medical Descriptors:
*cell adhesion
*protein binding

*protein domain
*laminin G like domain
binding affinity
umbilical vein
endothelium cell
protein protein interaction
protein secretion
cell activity
mammal cell
insect cell
Drosophila
human
nonhuman
controlled study
human cell
animal cell
article
priority journal
Drug Descriptors:
*laminin alpha4
*laminin
*syndecan
*glypican
glutathione transferase
protein LG1
protein LG2
protein LG4
protein LG5
heparin
heparan sulfate
heparitinase
heparin binding protein
hybrid protein
phospholipase C
dally like protein
laminin 8
cell protein
enzyme
Wnt protein
fibroblast growth factor
unclassified drug

L33 ANSWER 30 OF 33 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004449529 EMBASE
TI Heparan sulphate proteoglycans interact with neurocan and promote neurite outgrowth from cerebellar granule cells.
AU Akita K.; Toda M.; Hosoki Y.; Inoue M.; Fushiki S.; Oohira A.; Okayama M.; Yamashina I.; Nakada H.
CS H. Nakada, Department of Biotechnology, Faculty of Engineering, Kyoto Sangyo University, Kita-ku, Kyoto 603-8555, Japan. hnakada@cc.kyoto-su.ac.jp
SO Biochemical Journal, (1 Oct 2004) Vol. 383, No. 1, pp. 129-138.
Refs: 38
ISSN: 0264-6021 CODEN: BIJOAK
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English

ED Entered STN: 20041112
Last Updated on STN: 20041112

AB We found that neurocan, a major brain chondroitin sulphate proteoglycan, interacts with HSPGs (heparan sulphate proteoglycans) such as syndecan-3 and **glypican-1.** Binding of these HSPGs to neurocan was prevented by treatment of the HSPGs with heparitinases I and II, but not by treatment of neurocan with chondroitinase ABC. Scatchard plot analysis indicated that neurocan has two binding sites for these HSPGs with different affinities. It is known that neurocan in the rodent brain is proteolytically processed with aging into N- and C-terminal fragments. When a mixture of whole neurocan and N- and C-terminal fragments prepared from neonatal mouse brains or recombinant N- and C-terminal fragments was applied to a heparin column, the whole molecule and both the N- and C-terminal fragments bound to heparin. A centrifugation cell adhesion assay indicated that both the N- and C-terminal neurocan fragments could interact with these HSPGs expressed on the cell surface. To examine the biological significance of the HSPG-neurocan interaction, cerebellar granule cells expressing these HSPGs were cultured on the recombinant neurocan substrate. A significant increase in the rate of neurite outgrowth was observed on the wells coated with the C-terminal neurocan fragment, but not with the N-terminal one. Neurite outgrowth-promoting activity was inhibited by pre-treatment of neurocan substrate with heparin or the addition of heparitinase I to culture medium. These results suggest that HSPGs such as syndecan-3 and **glypican-1** serve as the cell-surface receptor of neurocan, and that the interaction of these HSPGs with neurocan through its C-terminal domain is involved in the promotion of neurite outgrowth.

CT Medical Descriptors:
*protein interaction
*nerve fiber growth
*granule cell
cerebellum cortex
protein binding
Scatchard plot
binding site
binding affinity
protein degradation
protein processing
aging
amino terminal sequence
carboxy terminal sequence
protein protein interaction
protein expression
cell surface
nerve cell culture
culture medium
protein domain
nonhuman
mouse
rat
controlled study
animal cell
newborn
article
priority journal
Drug Descriptors:
*proteoheparan sulfate: EC, endogenous compound
*neurocan: EC, endogenous compound
proteochondroitin sulfate: EC, endogenous compound
syndecan 3

glypican
glypican 1
heparin lyase
heparinase I
heparinase II
chondroitin ABC lyase
heparin
cell surface receptor
neurocan binding protein
unclassified drug

L33 ANSWER 31 OF 33 EMBASE
on STN
AN 2004013298 EMBASE
TI Vitronectin's basic domain is a syndecan ligand which functions in trans to regulate vitronectin turnover.
AU Wilkins-Port C.E.; Sanderson R.D.; Tominna-Sebald E.; McKeown-Longo P.J.
CS Dr. P.J. McKeown-Longo, Ctr. for Cell Biol./Cancer Research, Albany Medical College, 47 New Scotland Avenue, Albany, NY 12208, United States. mckeowp@mail.amc.edu
SO Cell Communication and Adhesion, (2003) Vol. 10, No. 2, pp. 85-103.
Refs: 97
ISSN: 1541-9061 CODEN: CCAEBH
CY United States
DT Journal; General Review
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20040116
Last Updated on STN: 20040116
AB During the process of tissue remodeling, vitronectin (Vn) is deposited in the extracellular matrix where it plays a key role in the regulation of pericellular proteolysis and cell motility. In previous studies we have shown that extracellular levels of vitronectin are controlled by receptor-mediated endocytosis and that this process is dependent upon vitronectin binding to sulfated proteoglycans. We have now identified vitronectin's 12 amino acid "basic domain" which is contained within the larger 40 amino acid heparin binding domain, as a syndecan binding site. Recombinant vitronectins representing wild type vitronectin (rVn) and vitronectin with the basic domain deleted (rVnΔ347-358) were prepared in a baculoviral expression system. The rVn as well as a glutathione S-transferase (GST) fusion protein, consisting of vitronectin's 40 amino acid heparin binding domain (GST-VnHBD), exhibited dose dependent binding to HT-1080 cell surfaces, which was attenuated following deletion of the basic domain. In addition, GST-VnHBD supported both HT-1080 and dermal fibroblast cell adhesion, which was also dependent upon the basic domain. Similarly, ARH-77 cells transfected with syndecans -1, -2, or -4, but not **Glypican-1**, adhered to GST-VnHBD coated wells, while adhesion of these same cells was lost following deletion of the basic domain. HT-1080 cells were unable to degrade rVnΔ347-358. Degradation of rVnΔ347-358 was completely recovered in the presence of GST-VnHBD but not in the presence of GST-VnHBDΔ347-358. These results indicate that turnover of soluble vitronectin requires ligation of vitronectin's basic domain and that this binding event can work in trans to regulate vitronectin degradation.
CT Medical Descriptors:
*cell adhesion
protein metabolism
protein domain

protein function
regulatory mechanism
extracellular matrix
protein analysis
sequence analysis
binding site
wild type
Baculovirus
virus vector
gene expression
gene deletion
cell surface
fibroblast
skin cell
cell line
protein binding
genetic transfection
protein degradation
amino acid sequence
human
nonhuman
controlled study
human cell
review
priority journal
Drug Descriptors:
*vitronectin: EC, endogenous compound
*syndecan: EC, endogenous compound
heparin binding protein: EC, endogenous compound
glutathione transferase: EC, endogenous compound
hybrid protein: EC, endogenous compound
recombinant protein
syndecan 1: EC, endogenous compound
syndecan 2: EC, endogenous compound
syndecan 4: EC, endogenous compound
glypican: EC, endogenous compound

L33 ANSWER 32 OF 33 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2003390046 EMBASE
TI The contribution of in vivo manipulation of gene expression to the understanding of the function of glypicans.
AU Filmus J.
CS J. Filmus, Sunnybrook/Women's Coll. Hlth. S., 2075 Bayview Ave., Toronto, Ont. M4N 3M5, Canada. jorge.filmus@swchsc.on.ca
SO Glycoconjugate Journal, (2002) Vol. 19, No. 4-5, pp. 319-323.
Refs: 47
ISSN: 0282-0080 CODEN: GLJOEW
CY Netherlands
DT Journal; General Review
FS 021 Developmental Biology and Teratology
029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20031009
Last Updated on STN: 20031009
AB The name glypican identifies a family of **heparan sulfate proteoglycans** that are linked to the cell surface by a **glycosylphosphatidylinositol** anchor. Members of this family have been identified in Drosophila, zebrafish, and mammals. The interest in

the study of glypicans has increased in the last few years as a result of the discovery that the glypican-3 gene (GPC-3) is mutated in an overgrowth and dysmorphic syndrome. Despite the increased interest, our knowledge about the function of glypicans is still limited, since the molecular basis for the role of glypican-3 in the regulation of body size remains unknown. The in vivo manipulation of glypican expression in lower organisms, however, has demonstrated that these proteoglycans can modulate cellular responses to Wnts and bone morphogenetic factors. Future studies should investigate whether the phenotype of GPC-3-deficient individuals is also due to altered modulation of cellular responses to these factors.

CT Medical Descriptors:
*gene expression regulation
*gene function
protein analysis
gene interaction
tissue specificity
protein synthesis
protein function
zebra fish
cell polarity
cell structure
morphogenesis
craniofacial malformation
cell mutant
concentration response
genetic manipulation
protein expression
Simpson Golabi Behmel syndrome
prenatal period
perinatal period
clinical feature
genetic risk
gene mutation
nonhuman
review
priority journal
Drug Descriptors:
*glypican 3: EC, endogenous compound
*glypican: EC, endogenous compound
*glycoprotein: EC, endogenous compound
Wnt protein: EC, endogenous compound
somatomedin binding protein 2: EC, endogenous compound
somatomedin binding protein 1: EC, endogenous compound
bone morphogenetic protein 4: EC, endogenous compound
unclassified drug

L33 ANSWER 33 OF 33 EMBASE
on STN
AN 2000408889 EMBASE
TI Cellular components that functionally interact with signaling phospholipase A2s.
AU Murakami M.; Nakatani Y.; Kuwata H.; Kudo I.
CS M. Murakami, Department of Health Chemistry, School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan
SO Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, (31 Oct 2000) Vol. 1488, No. 1-2, pp. 159-166.
Refs: 54
ISSN: 1388-1981 CODEN: BBMLFG
PUI S 1388-1981(00)00118-9

CY Netherlands
DT Journal; General Review
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 20001214
Last Updated on STN: 20001214
AB Accumulating evidence has suggested that cytosolic phospholipase A2 (cPLA2) and several secretory PLA2 (sPLA2) isozymes are signaling PLA2s that are functionally coupled with downstream cyclooxygenase (COX) isozymes for prostaglandin (PG) biosynthesis. Arachidonic acid (AA) released by cPLA2 and sPLA2s is supplied to both COX-1 and COX-2 in the immediate, and predominantly to COX-2 in the delayed, PG-biosynthetic responses. Vimentin, an intermediate filament component, acts as a functional perinuclear adapter for cPLA2, in which the C2 domain of cPLA2 associates with the head domain of vimentin in a Ca2+ -sensitive manner. The heparin-binding signaling sPLA2-IIA, IID and V bind the **glycosylphosphatidylinositol**-anchored **heparan sulfate proteoglycan** glypican, which plays a role in sorting of these isozymes into caveolae and perinuclear compartments. Phospholipid scramblase, which facilitates transbilayer movement of anionic phospholipids, renders the cellular membranes more susceptible to signaling sPLA2s. There is functional cooperation between cPLA2 and signaling sPLA2s in that prior activation of cPLA2 is required for the signaling sPLA2s to act properly. cPLA2-derived AA is oxidized by 12/15-lipoxygenase, the products of which not only augment the induction of sPLA2 expression, but also cause membrane perturbation, leading to increased cellular susceptibility to the signaling sPLA2 s. sPLA2-X, a heparin-non-binding sPLA2 isozyme, is capable of releasing AA from intact cells in the absence of cofactors. This property is attributed to its ability to avidly hydrolyze zwitterionic phosphatidylcholine, a major phospholipid in the outer plasma membrane. sPLA2-V can also utilize this route in several cell types. Taken together, the AA-releasing function of sPLA2s depends on the presence of regulatory cofactors and interfacial binding to membrane phospholipids, which differ according to cell type, stimuli, secretory processes, and subcellular distributions. (C) 2000 Elsevier Science B.V.
CT Medical Descriptors:
*cell composition
*protein interaction
signal transduction
cytosol
prostaglandin synthesis
enzyme release
cell membrane
enzyme activation
cell interaction
enzyme metabolism
protein expression
hydrolysis
cell type
cellular distribution
cell secretion
nonhuman
review
priority journal
Drug Descriptors:
*phospholipase A2: EC, endogenous compound
isoenzyme: EC, endogenous compound
prostaglandin synthase: EC, endogenous compound

prostaglandin: EC, endogenous compound
arachidonic acid: EC, endogenous compound
cyclooxygenase 1: EC, endogenous compound
cyclooxygenase 2: EC, endogenous compound
vimentin: EC, endogenous compound
calcium ion: EC, endogenous compound
heparin binding protein: EC, endogenous compound
glycosylphosphatidylinositol: EC, endogenous compound
heparan sulfate: EC, endogenous compound
scramblase: EC, endogenous compound
phosphatidylcholine: EC, endogenous compound
membrane phospholipid: EC, endogenous compound

=> □
=>

=> d his ful inverter search

(FILE 'HOME' ENTERED AT 14:55:22 ON 12 SEP 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, HCAPLUS' ENTERED AT 14:55:37 ON 12 SEP 2005
E LANDER A/AU
L1 371 SEA ABB=ON PLU=ON ("LANDER A"/AU OR "LANDER A B"/AU OR "LANDER A D"/AU OR "LANDER A J"/AU OR "LANDER A K"/AU OR "LANDER A V"/AU) OR ("LANDER ARTHUR"/AU OR "LANDER ARTHUR D"/AU OR "LANDER ARTHUR G"/AU OR "LANDER ARTHUR M"/AU)
L*** DEL 697 S KORC M/AU
E KORC M/AU
L*** DEL 26962 S E3-4 OR 310
L*** DEL 27321 S L1 OR L2
L2 1033 SEA ABB=ON PLU=ON ("KORC M"/AU OR "KORC M E"/AU) OR "KORC MURRAY"/AU
L3 1383 SEA ABB=ON PLU=ON L1 OR L2
L4 1492 SEA ABB=ON PLU=ON GLYPICAN#
L5 81 SEA ABB=ON PLU=ON L3 AND L4
L6 5183504 SEA ABB=ON PLU=ON ?CANCER? OR ?TUMOR? OR ?CARCINOMA? OR ?NEOPLAS?
L7 5353674 SEA ABB=ON PLU=ON (?CANCER? OR ?TUMOR? OR ?CARCINOMA? OR ?NEOPLAS?)/BI

FILE 'CANCERLIT' ENTERED AT 14:58:29 ON 12 SEP 2005
E LANDER A/AU
L8 17 SEA ABB=ON PLU=ON ("LANDER A"/AU OR "LANDER A D"/AU)
E KORC M/AU
L9 141 SEA ABB=ON PLU=ON ("KORC M"/AU OR "KORC MURRAY"/AU)
L10 153 SEA ABB=ON PLU=ON L9 OR L8
L11 1283830 SEA ABB=ON PLU=ON ?CANCER? OR ?TUMOR? OR ?CARCINOMA? OR ?NEOPLAS?
L12 129 SEA ABB=ON PLU=ON L11 AND L10

FILE 'MEDLINE, EMBASE, BIOSIS, HCAPLUS' ENTERED AT 14:59:48 ON 12 SEP 2005
L13 36 SEA ABB=ON PLU=ON L5 AND L7

FILE 'CANCERLIT, MEDLINE, EMBASE, BIOSIS, HCAPLUS' ENTERED AT 14:59:58 ON 12 SEP 2005
L14 137 DUP REM L12 L13 (28 DUPLICATES REMOVED)
ANSWERS '1-129' FROM FILE CANCERLIT
ANSWERS '130-132' FROM FILE MEDLINE
ANSWERS '133-135' FROM FILE BIOSIS
ANSWERS '136-137' FROM FILE HCAPLUS
D TI 1-10
L15 361 SEA ABB=ON PLU=ON GLYPICAN# (2W) 1
L16 10 SEA ABB=ON PLU=ON L14 AND L15
D TI 1-10
D ALL 4

FILE HOME

FILE MEDLINE
FILE LAST UPDATED: 11 SEP 2005 (20050911/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 9 Sep 2005 (20050909/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 8 September 2005 (20050908/ED)

FILE RELOADED: 19 October 2003.

FILE HCAPLUS

FILE COVERS 1907 - 12 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 11 Sep 2005 (20050911/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> fil cancerlit medline embase biosis hcaplus
FILE 'CANCERLIT' ENTERED AT 15:02:39 ON 12 SEP 2005

FILE 'MEDLINE' ENTERED AT 15:02:39 ON 12 SEP 2005

FILE 'EMBASE' ENTERED AT 15:02:39 ON 12 SEP 2005
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=> d que l16
L1          371 SEA ("LANDER A"/AU OR "LANDER A B"/AU OR "LANDER A D"/AU OR
                "LANDER A J"/AU OR "LANDER A K"/AU OR "LANDER A V"/AU) OR
                ("LANDER ARTHUR"/AU OR "LANDER ARTHUR D"/AU OR "LANDER ARTHUR
                G"/AU OR "LANDER ARTHUR M"/AU)
L2         1033 SEA ("KORC M"/AU OR "KORC M E"/AU) OR "KORC MURRAY"/AU
L3         1383 SEA L1 OR L2
L4         1492 SEA GLYPICAN#
L5           81 SEA L3 AND L4
L7      5353674 SEA (?CANCER? OR ?TUMOR? OR ?CARCINOMA? OR ?NEOPLAS?)/BI
L8           17 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ("LANDER A"/AU OR "LANDER A
                D"/AU)
L9          141 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ("KORC M"/AU OR "KORC
                MURRAY"/AU)
L10         153 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L9 OR L8
L11     1283830 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ?CANCER? OR ?TUMOR? OR
                ?CARCINOMA? OR ?NEOPLAS?
L12         129 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L11 AND L10
L13          36 SEA L5 AND L7
L14         137 DUP REM L12 L13 (28 DUPLICATES REMOVED)
L15         361 SEA GLYPICAN# (2W) 1
L16          10 SEA L14 AND L15


=> d bib ab l16 1-10

L16  ANSWER 1 OF 10  CANCERLIT on STN
AN   2002067184     CANCERLIT
DN   21347237   PubMed ID: 11454708
TI   Glypican-1 is overexpressed in human breast
     cancer and modulates the mitogenic effects of multiple
     heparin-binding growth factors in breast cancer cells.
AU   Matsuda K; Maruyama H; Guo F; Kleeff J; Itakura J; Matsumoto Y;
     Lander A D; Korc M
CS   Division of Endocrinology, Diabetes and Metabolism, Department of
     Medicine, Biological Chemistry, and Pharmacology, University of
     California, Irvine, California 92697, USA.
NC   CA-40162 (NCI)
     NS-26862 (NINDS)
SO   CANCER RESEARCH, (2001 Jul 15) 61 (14) 5562-9.
     Journal code: 2984705R. ISSN: 0008-5472.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
```

LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2001407894
EM 200108
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB Glypicans are a family of glycosylphosphatidylinositol-anchored cell surface heparan sulfate proteoglycans implicated in the control of cellular growth and differentiation. Here we show that **glypican-1** is strongly expressed in human breast **cancers**, whereas expression of **glypican-1** is low in normal breast tissues. In contrast, the expression of glypican-3 and -4 is only slightly increased in breast **cancers** by comparison with normal breast tissues, and glypican-2 and -5 are below the level of detection by Northern blotting in both normal and **cancer** samples. Treatment of MDA-MB-231 and MDA-MB-468 breast **cancer** cells with phosphoinositide-specific phospholipase-C abrogated the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor and fibroblast growth factor 2. Stable transfection of these cells with a **glypican-1** antisense construct markedly decreased **glypican-1** protein levels and the mitogenic response to the same heparin-binding growth factors, as well as that to heregulin alpha, heregulin beta, and hepatocyte growth factor. Syndecan-1 was also expressed at high levels in both breast **cancer** tissues and breast **cancer** cells when compared with normal breast tissues. There was a good correlation between **glypican-1** and syndecan-1 expression in the **tumors.** However, clones expressing the **glypican-1** antisense construct did not exhibit decreased syndecan-1 levels, indicating that loss of responsiveness to heparin-binding growth factors in these clones was not due to altered syndecan-1 expression. Furthermore, 8 of 10 **tumors** with stage 2 or 3 disease exhibited high levels of **glypican-1** by Northern blot analysis. In contrast, low levels of **glypican-1** mRNA were evident in 1 of 10 **tumors** with stage 2 or 3 disease and in 9 of 10 **tumors** with stage 1 disease. Taken together, these data suggest that **glypican-1** may play a pivotal role in the ability of breast **cancer** cells to exhibit a mitogenic response to multiple heparin-binding growth factors and may contribute to disease progression in this malignancy.

L16 ANSWER 2 OF 10 CANCERLIT on STN
AN 1999433578 CANCERLIT
DN 99433578 PubMed ID: 10505759
TI Stable transfection of a **glypican-1** antisense construct decreases **tumorigenicity** in PANC-1 pancreatic **carcinoma** cells.
AU Kleeff J; Wildi S; Kumbasar A; Friess H; **Lander A D**; **Korc M**
CS Department of Medicine, University of California, Irvine 92697, USA.
NC CA-40162 (NCI)
SO PANCREAS, (1999 Oct) 19 (3) 281-8.
Journal code: 8608542. ISSN: 0885-3177.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1999433578
EM 199911
ED Entered STN: 20000221

Last Updated on STN: 20000221
AB **Glypican-1** belongs to a family of glycosylphosphatidylinositol (GPI)-anchored heparan sulfate proteoglycans (HSPGs) that affect cell growth, invasion, and adhesion. Cell-surface HSPGs are believed to act as co-receptors for heparin-binding mitogenic growth factors. It was reported that **glypican-1** is strongly expressed in human pancreatic **cancer**, and that it may play an essential role in regulating growth-factor responsiveness in pancreatic **carcinoma** cells. In this study we investigated the effects of decreased **glypican-1** expression in PANC-1 pancreatic **cancer** cells. To this end, PANC-1 cells were stable transfected with a full-length **glypican-1** antisense construct. The glypican- antisense transfected clones displayed markedly reduced glypican- protein levels and a marked attenuation of the mitogenic responses to heparin-binding growth factors that are commonly overexpressed in pancreatic **cancer**: fibroblast growth factor-2 (FGF2), heparin-binding epidermal growth factor (EGF)-like growth factor (HB-EGF), and hepatocyte growth factor (HGF). In addition, **glypican-1** antisense-expressing PANC-1 cells exhibited a significantly reduced ability to form **tumors** in nude mice in comparison with parental and sham-transfected PANC-1 cells. These data suggest that **glypican-1** plays an important role in the responses of pancreatic **cancer** cells to heparin-binding growth factors, and documents for the first time that its expression may enhance **tumorigenic** potential in vivo.

L16 ANSWER 3 OF 10 CANCERLIT on STN
AN 1999021665 CANCERLIT
DN 99021665 PubMed ID: 9802880
TI The cell-surface heparan sulfate proteoglycan **glypican-1** regulates growth factor action in pancreatic **carcinoma** cells and is overexpressed in human pancreatic **cancer.**
AU Kleeff J; Ishiwata T; Kumbasar A; Friess H; Buchler M W; **Lander A D; Korc M**
CS Departments of Medicine, Biological Chemistry, and Pharmacology, University of California, 92697, USA.
NC CA-40162 (NCI)
NS-26862 (NINDS)
SO JOURNAL OF CLINICAL INVESTIGATION, (1998 Nov 1) 102 (9) 1662-73. Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Abridged Index Medicus Journals; Priority Journals
OS MEDLINE 1999021665
EM 199812
ED Entered STN: 19990127
Last Updated on STN: 19990127
AB Heparan sulfate proteoglycans (HSPGs) play diverse roles in cell recognition, growth, and adhesion. In vitro studies suggest that cell-surface HSPGs act as coreceptors for heparin-binding mitogenic growth factors. Here we show that the glycosylphosphatidylinositol- (GPI-) anchored HSPG **glypican-1** is strongly expressed in human pancreatic **cancer**, both by the **cancer** cells and the adjacent fibroblasts, whereas expression of **glypican-1** is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic **cancer** cell lines, which express **glypican-1**, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors that are commonly overexpressed in

pancreatic **cancer**: fibroblast growth factor 2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). PI-PLC did not alter the response to the non-heparin-binding growth factors EGF and IGF-1. Stable expression of a form of **glypican-1** engineered to possess a transmembrane domain instead of a GPI anchor conferred resistance to the inhibitory effects of PI-PLC on growth factor responsiveness. Furthermore, transfection of a **glypican-1** antisense construct attenuated **glypican-1** protein levels and the mitogenic response to FGF2 and HB-EGF. We propose that **glypican-1** plays an essential role in the responses of pancreatic **cancer** cells to certain mitogenic stimuli, that it is relatively unique in relation to other HSPGs, and that its expression by pancreatic **cancer** cells may be of importance in the pathobiology of this disorder.

L16 ANSWER 4 OF 10 CANCERLIT on STN
AN 1998380514 CANCERLIT
DN 98380514 PubMed ID: 9712917
TI Heparan sulfate proteoglycans as adhesive and anti-invasive molecules. Syndecans and glypican have distinct functions.
AU Liu W; Litwack E D; Stanley M J; Langford J K; **Lander A D**; Sanderson R D
CS Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA.
NC CA 55879 (NCI)
CA 68494 (NCI)
NS 26862 (NINDS)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Aug 28) 273 (35) 22825-32. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 1998380514
EM 199809
ED Entered STN: 19981007
Last Updated on STN: 19981007
AB ARH-77 cells do not adhere to type I collagen and readily invade into collagen gels, but following expression of the transmembrane heparan sulfate proteoglycan syndecan-1, they bind collagen and fail to invade. We now show that cells transfected with syndecan-2 or syndecan-4 also bind collagen and are non-invasive. In contrast, cells transfected with the glycosylphosphatidylinositol-anchored proteoglycan **glypican-1** do not bind to collagen and remain invasive, even though glypican- and syndecan-expressing cells have similar surface levels of heparan sulfate, and their proteoglycans have similar affinities for collagen. Analysis of cells expressing syndecan-1-**glypican-1** chimeric proteoglycans reveals that inhibition of invasion requires the extracellular domain of syndecan but not its transmembrane or cytoplasmic domain. Surprisingly, cells bearing a chimera composed of the glypican extracellular domain fused to the syndecan transmembrane and cytoplasmic domains bind to collagen but remain invasive, implying that adhesion to collagen is not by itself sufficient to inhibit invasion. Apparently, the extracellular domain of syndecan-1, presumably by interacting with cell-surface signal transducing molecules, directly regulates complex cell behaviors such as motility and invasiveness. These results also show for the first time that syndecans and glypicans can have distinct functions, even when expressed by the same cell type.

L16 ANSWER 5 OF 10 MEDLINE on STN
AN 2004407113 MEDLINE
DN PubMed ID: 15294952
TI Membrane-associated heparan sulfate proteoglycans are involved in the recognition of cellular targets by NKp30 and NKp46.
AU Bloushtain Noga; Qimron Udi; Bar-Ilan Ahuva; Hershkovitz Oren; Gazit Roi; Fima Eyal; **Korc Murray**; Vlodavsky Israel; Bovin Nicolai V; Porgador Angel
CS Department of Microbiology and Immunology, Faculty of Health Sciences, and the Cancer Research Center, Ben Gurion University of the Negev, Beer Sheva, Israel.
SO Journal of immunology (Baltimore, Md. : 1950), (2004 Aug 15) 173 (4) 2392-401.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200409
ED Entered STN: 20040818
Last Updated on STN: 20040929
Entered Medline: 20040928
AB Lysis of virus-infected and **tumor** cells by NK cells is mediated via natural cytotoxicity receptors (NCRs). We have recently shown that the NKp44 and NKp46 NCRs, but not the NKp30, recognize viral hemagglutinins. In this study we explored the nature of the cellular ligands recognized by the NKp30 and NKp46 NCRs. We demonstrate that target cell surface heparan sulfate proteoglycans (HSPGs) are recognized by NKp30 and NKp46 and that 6-O-sulfation and N-acetylation state of the glucose building unit affect this recognition and lysis by NK cells. **Tumor** cells expressing cell surface heparanase, CHO cells lacking membranal heparan sulfate and **glypican-1**-suppressed pancreatic **cancer** cells manifest reduced recognition by NKp30 and NKp46 and are lysed to a lesser extent by NK cells. Our results are the first clue for the identity of the ligands for NKp30 and NKp46. Whether the ligands are particular HSPGs, unusual heparan sulfate epitopes, or a complex of HSPGs and either other protein or lipid moieties remains to be further explored.

L16 ANSWER 6 OF 10 MEDLINE on STN
AN 2004346086 MEDLINE
DN PubMed ID: 15249209
TI **Glypican-1** antisense transfection modulates TGF-beta-dependent signaling in Colo-357 pancreatic **cancer** cells.
AU Li Junsheng; Kleeff Jorg; Kayed Hany; Felix Klaus; Penzel Roland; Buchler Markus W; **Korc Murray**; Friess Helmut
CS Department of General Surgery, University of Heidelberg, Heidelberg, Germany.
NC CA-10130 (NCI)
CA-75059 (NCI)
SO Biochemical and biophysical research communications, (2004 Aug 6) 320 (4) 1148-55.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 20040714

Last Updated on STN: 20040911
Entered Medline: 20040910

AB The heparan sulfate proteoglycan **glypican-1** is essential as a co-receptor for heparin binding growth factors, such as HB-EGF and FGF-2, in pancreatic **cancer** cells. In the present study, the role of **glypican-1** in the regulation of TGF-beta signaling was investigated. Colo-357 pancreatic **cancer** cells were stably transfected with a full-length **glypican-1** antisense construct. Cell growth was determined by MTT and soft agar assays. TGF-beta1 induced p21 expression and Smad2 phosphorylation were analyzed by immunoblotting. PAI-1 promoter activity was determined by luciferase assays. Down-regulation of **glypican-1** expression by stable transfection of a full-length **glypican-1** antisense construct resulted in decreased anchorage-dependent and -independent cell growth in Colo-357 pancreatic **cancer** cells and attenuated TGF-beta1 induced cell growth inhibition, Smad2 phosphorylation, and PAI-1 promoter activity. There was, however, no significant difference in TGF-beta1 induced p21 expression and Smad2 nuclear translocation. In conclusion, **glypican-1** is required for efficient TGF-beta1 signaling in pancreatic **cancer** cells.

L16 ANSWER 7 OF 10 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:518654 BIOSIS
DN PREV200200518654
TI Overexpression of FGF type I receptor enhances surface retention of **glypican-1** and FGF-2 dependent signaling.
AU Matsuda, Kei [Reprint author]; Lopez, Martha [Reprint author]; Fukahi, Kimi [Reprint author]; **Lander, Arthur** [Reprint author]; **Korc, Murray** [Reprint author]
CS Irvine, CA, USA
SO Gastroenterology, (April, 2002) Vol. 122, No. 4 Suppl. 1, pp. A-139. print.
Meeting Info.: Digestive Disease Week and the 103rd Annual Meeting of the American Gastroenterological Association. San Francisco, CA, USA. May 19-22, 2002.
CODEN: GASTAB. ISSN: 0016-5085.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

L16 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2002:419974 BIOSIS
DN PREV200200419974
TI Growth factors and signaling events in pancreatic **cancer.**
AU **Korc, Murray** [Reprint author]
CS University of California, Irvine, CA, USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 1170. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002

L16 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:435071 HCAPLUS
DN 139:3235
TI **Glypican-1** determination and modulation in human breast **cancer** diagnosis and treatment
IN **Korc, Murray; Lander, Arthur D.**
PA USA
SO U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 807,575.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003103980	A1	20030605	US 2002-210327	20020731
WO 2000023109	A1	20000427	WO 1999-US24176	19991015

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	US 1998-104510P	P	19981016
	US 1999-121624P	P	19990225
	WO 1999-US24176	W	19991015
	US 2001-807575	A2	20010712
	US 2001-309722P	P	20010731

AB Glycosylphosphatidylinositol- (GPI-) anchored heparan sulfate proteoglycan (HSPG) glypican-1 is strongly expressed in human breast and pancreatic **cancer**-both by the **cancer** cells and, in the case of pancreatic **cancer**, the adjacent fibroblasts-whereas expression of glypican-1 is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic **cancer** cell lines, which express glypican-1, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast **cancer** cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast **cancer** tissues as well as breast **cancer** cells by comparison with breast normal tissues. Temporary or permanent transfection of a glypican-1 antisense construct attenuated glypican-1 protein levels and the mitogenic response to FGF2 and HB-EGF. Glypican can be used to detect the **carcinoma** in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense constructs) of surface of the extracellular domain of glypican-1 are effective in retarding the growth of glypican-responsive **carcinomas.** By immunohistochem., strong glypican-1 immunoreactivity was present in a heterogeneous pattern in the **cancer** cells forming intraductal and lobular **carcinomas**, and in the fibroblasts surrounding the **cancer** cells but not in the fibroblasts that were more distant from the **tumor.** A moderate to strong glypican-1 mRNA in situ hybridization signal was also present in the **cancer** cells, and, to a lesser extent, in the fibroblasts immediately adjacent to the **cancer** cells. These

observations suggest that breast **cancer** cells produce and release glypican-1, and that some of the glypican-1 present in the fibroblasts surrounding the breast **cancer** cells in vivo derives from the **cancer** cells.

L16 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:277880 HCAPLUS
DN 132:305482
TI **Glypicans** for the detection and treatment of human **carcinoma**
IN **Lander, Arthur; Korc, Murray**
PA The Regents of the University of California, USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000023109	A1	20000427	WO 1999-US24176	19991015
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2346264	AA	20000427	CA 1999-2346264	19991015
	EP 1146903	A1	20011024	EP 1999-954963	19991015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AU 769125	B2	20040115	AU 2000-11181	19991015
	US 2003103980	A1	20030605	US 2002-210327	20020731
PRAI	US 1998-104510P	P	19981016		
	US 1999-121624P	P	19990225		
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AB Glycosylphosphatidylinositol- (GPI-) anchored HSPG glypican-1 is strongly expressed in human breast and pancreatic **cancer** - both by the **cancer** cells and in the case of pancreatic **cancer** the adjacent fibroblasts - whereas expression of glypican-1 is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic **cancer** cell lines, which express glypican-1, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast **cancer** cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast **cancer** tissues as well as breast **cancer** cells by comparison with breast normal tissues. Temporary or permanent transfection of a glypican-1 antisense construct attenuated glypican-1 protein levels and the mitogenic response to FGF2 and HB-EFG. Glypican can be used to detect the **carcinoma** in vitro and therapeutics that either bind to (e.g., antibodies or drugs), remove (e.g., enzymes) or prevent the expression (e.g., antisense

constructs) of surface of the extracellular domain of glypican-1 are effective in retarding the growth of glypican-responsive **carcinomas.**

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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